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CHEMICAL BURNS OF THE HUMAN CORNEA

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A chemical burn of the cornea is defined as an injury which results from local contact with a chemical (solid, liquid, or vapor) to such a degree that there is alteration in the structure of the cornea and the conjunctiva. This alteration in structure is demonstrated by a positive stain when a 2-percent buffered solution of fluorescein is applied.

It has been the experience of the author to have practiced industrial ophthalmology in an industrial center where a large variety of chemicals is manufactured and utilized. These include particularly many of the newer solvents, plastics, alcohols, aldehydes, and hydrocarbons, as well as the intermediates involved in their manufacture. The observations discussed in this paper have been made through association with such establishments as Carbide and Carbon Chemicals Corporation, American Viscose Corporation, Westvaco Chlorine Products Corporation, Monsanto Chemicals, Ohio-Apex, and Belle Alkali Companies. The Carbide and Carbon Chemicals Corporation alone manufactures and ships over 200 different chemical compounds from their local operations, and it has been this firm which has sponsored and aided the present study. A companion paper[1] is presented on adjoining pages by the Chemical Hygiene Fellowship at the Mellon Institute, Pittsburgh, which is supported by that corporation. That communication presents a tabulation of some 180 chemicals arranged according to the severity of injury they produce on the cornea of the albino rabbit, together with studies of burns of the rabbit cornea which have thrown light upon clinical observation.

The magnitude of the problem in one plant is shown by the data in Table 1. Each one of the patients in the cases listed was known to have had a chemical exposure which was at least severe enough to bring the employee to the dispensary, complaining of his eyes and requiring treatment. As can be seen, only 10 percent of the injuries were severe enough to be referred to the ophthalmologist, and, in this particular group, only one case was terminated with a loss of vision. In all of those treated in the dispensary, there was complete recovery. In a recent tabulation for 12 months in the same establishment, it was found that 52 percent of the chemical eye injuries were caused by vapors and mists,

TABLE 1

EXPERIENCE OF ONE PLANT WITH CHEMICAL EYE IRRITATIONS AND BURNS, EXCLUSIVE OF TRAUMATIC INJURY

Year	Dispensary Cases	Referred Cases
1942	663	85
1943	583	69
1944	926	82
1945	1,394	97
Totals	3,566	333

31 percent by liquids, and 17 percent by solids. In due respect to the Safety Department of the corporation, it should be remembered that during a great portion of the period the plant was operating under wartime conditions with inexperienced, and in some cases inefficient, help, due to loss of regular employees to the Armed Services.

Every endeavor has been made to cooperate closely with plant Safety and Medical Departments in order to maintain an adequate program for the prevention and treatment of chemical burns of the eye.

First-aid treatment

Over the period of seven years covered by this study, it has been determined, beyond question of doubt, that early

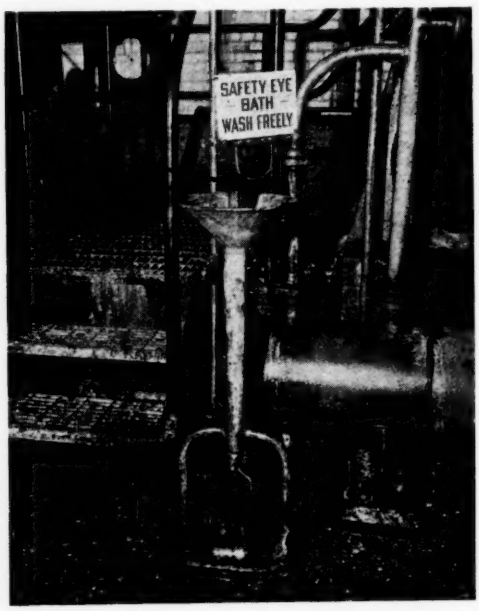

Fig. 1 (McLaughlin). Eye-washing fountain installed in a chemical unit. 1, Soft rubber eye piece; 2, foot peddle to control water flow.

treatment is of supreme importance to the ultimate outcome of a chemical burn of the eye.[2] Development of the following program has been accomplished, during this period, by Dr. Thomas W. Nale,[3] medical director of the South Charleston Operation of the Carbide and Carbon Chemicals Corporation, and by me. The results obtained lead us to believe that the following technique is most desirable:

The immediate treatment of an eye burn is at the site of the accident. Specially built foot-operated eyewashing fountains are provided close at hand in every working area (fig. 1). The injured eye is washed thoroughly and at once with tap water, holding the lids open with the hands. No neutralizing substances are used, since study[1] of this practice reveals that not only do they do no good but that actually some are injurious in themselves. After the preliminary washing, the victim is at once transported to the medical dispensary, where equipment for first aid is held ready at all times.

A list of chemicals used in the plant is maintained in each dispensary. This list sets forth the severity of injury expected, and the acidity, alkalinity, or neutrality of any chemical in question. The more frequently used chemicals were evaluated on the basis of experiments made in rabbits' eyes.[1] A similar list is in the hands of the ophthalmic consultant, so that he may have some basis for judging in advance the therapeutic measures called for.

When a chemical eye burn is brought into the dispensary, the patient is placed in a reclining chair (Beck) and tilted back over a catch basin. The eye is inspected and then anesthetized with 0.5-percent pontocaine solution. Gross particles are removed with a moist cotton applicator. The eye is then irrigated with a continuous flow of normal saline, no pressure being exerted on the eye. Special equipment (figs. 2 and 3) consists

of a 5-gallon bottle mounted on a movable stand and equipped with a siphon (3-foot head). Irrigation is continued for 15 minutes, after which the eye is reëxamined for gross particles and then stained with fluorescein. If the eye is damaged, the injured cells will take a typical fluorescent yellow-green stain. If a stain is observed, further anesthesia is produced with pontocaine, and washing proceeds for another 15 minutes. The stain is applied a second time and, if found to be positive, the case is considered to be an unequivocal chemical burn and is referred to the ophthalmologist. Time, here, is of importance, and it has been my experience that no more than two hours should elapse between the moment of the burn and the time when special treatment is rendered. Certainly, the prognosis grows worse as time passes, and a delay of six hours almost always results in some loss of vision.

It is possible to get moderately severe burns from vapors alone. In cases of vapor irritation, the same technique of emergency treatment is used as for other burns, except that it is not necessary to wash the eyes for as long, unless there is a demonstrable staining of the cornea. In all cases where washing is reduced to the first 15 minutes, a recheck of the eye is made with stain in two hours, and the patient is warned to report at once should any untoward symptoms develop in the suspected eye. This is done because a few chemicals have been observed to cause a delayed injury, producing a breakdown of corneal epithelium some hours after contact.

Denuding, a specialized technique

When I began the study of chemical burns of the eye, seven years ago, it was a debatable question whether or not some chemicals had a "delayed action." Such compounds frequently caused a loss of vision due to opacification of the cornea and adhesions of the conjunctiva, following a symptom-free period of several hours after accidental contact. In searching for a scientific basis for this behavior, the most notable finding was the change in corneal structure produced by all alkaline and a few neutral organic compounds, but not by acidic compounds nor those neutral chemicals which experience shows to be relatively harmless.

The corneal structure is best observed with the high power of the biomicroscope under retroillumination,[4] with occasional resort to direct illumination. The change consists in the presence of areas of opacity in the superficial layers of the corneal epithelium. They vary in size, possess a grayish tint, and have well-defined margins. They suggest keratitic deposits, but direct illumination reveals them to lie immediately posterior to the precorneal film[5] in the most superficial epithelial layers anterior to Bowman's membrane. The opaque areas are seen to be stained a faint green by fluorescein when observed by direct illumination.

We at first thought that the offending chemical had penetrated into the epithelial cells, there reacting with the cytoplasmic protein. However, this would bind the chemical in place and probably neutralize its ability to injure other cells. Studies reported by Carpenter and Smyth[1] make it appear more probable that the foreign compound initially is physically adsorbed upon protein structures of the corneal epithelium. Following this, a portion of the adsorbed chemical denatures cellular protein, resulting in necrosis. The remainder is liberated slowly with its chemical nature unchanged, to diffuse from the original site of adsorption into previously unaffected tissue. Therefore, instead of a delayed effect, there is a progressive action which may spread to involve the entire depth of the epithelium

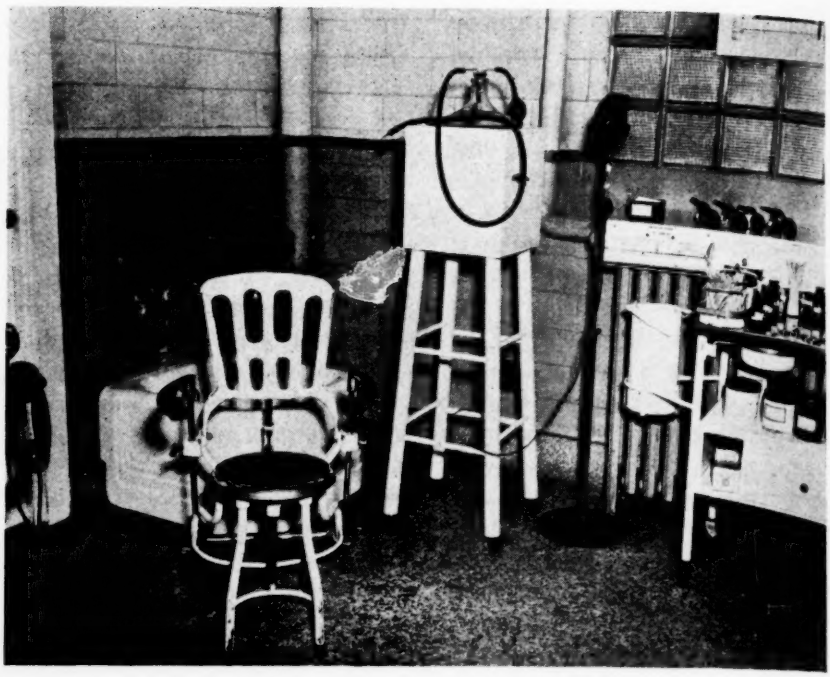

Fig. 2 (McLaughlin). Equipment utilized in irrigating chemical burns to the eye.

and, eventually, Bowman's membrane, at which point irreparable damage to the tissue results.

The greater number of chemicals behaving in this way are alkaline, and at first it appeared that neutralization of the compound bound to corneal epithelium would halt the progressive action. However, animal experiment[1] demonstrated no amelioration of injury from attempted neutralization. It was then apparent that only one form of treatment was possible, that of mechanical removal of the involved cells before a progressive action could be initiated. This operation is named "denuding." As carried out by me, the manipulation differs in purpose and thoroughness of control from débridement.

No evidence for a progressive action of acids has been observed. They apparently react rapidly with cell proteins, coagulating them, and themselves being neutralized in the process. The extent of an acid burn of the cornea is, of course, determined by the amount and concentration of acid in the eye and the length of time that elapses before it is washed out. The method generally used in treating an acid burn is to débride the dead tissue and treat the eye symptomatically. Following the appearance of the communication by Mann[6] on corneal healing, the author employed clinically the methods described and concluded, in conflict with her findings, that the course of healing is not prolonged by removing destroyed tissue. Furthermore, its removal reduces secondary infection by eliminating the substrate for bacterial growth. Consequently, I still consider débridement essential following corneal burns caused by acids.

The denuding technique in its early application consisted of complete removal of the epithelium down to Bowman's

membrane. The biomicroscopic picture of the completely denuded Bowman's membrane is that of a smooth surface, without evident cellular structure, having regularly placed, minute dimples which are the rami perforantes[7] of the corneal nerves. Although we have later shown that such radical removal of tissue is unnecessary, we do know that the epithelium is rapidly replaced, and we have seen indication that the two methods of regeneration described by Mann[6] are correct.

Denuding, as used today, removes only such part of the tissue as is involved, and the manipulation is controlled by repeated examination with the biomicroscope. The instrument of choice is a round tooth pick wound with cotton in the nature of a swab. The epithelium is softened with 4-percent cocaine-hydrochloride solution, which also acts as a local anesthetic. The applicator is started in the center of the involved area with just enough pressure to distort slightly the corneal surface. With a circular motion, the applicator is carried progressively from the center to the outside of the area, where it is lifted. This action is repeated over the entire affected area until the biomicroscope reveals no more of the clouded cells, but only a rough surface indicative of ruptured cell bodies and fragments of cells. After the corneal denuding is completed, a careful denuding of the conjunctiva is performed. Here the applicator is passed from the limbus to the cul-de-sacs, each lid swept from side to side, and the cul-de-sacs finally swept. The eye is then flushed with stainless solution of merthiolate, which acts not only to remove the denuding refuse, but also as an antiseptic.

Study of the eye during the denuding process may be confusing, for the precorneal film has been removed and allowance must be made for its absence. In the final check on the biomicroscope, the meniscus of the lacrimal fluid where it meets the lower lid should be observed carefully, and no cellular débris should be left. Each eye is routinely closed with 5-percent sulfathiazole ointment (sulfadiazene is equally efficacious) and a lid-immobilizing patch is applied.

Fig. 3 (McLaughlin). Demonstrating method of continuous irrigation of chemical burns to the cornea.

During the first consultation, special attention should be given to all possible foci of infection, especially the teeth. While treatment of the foci need not be started at this time, it is important that they be noted on the record. Treatment is started if the eye does not heal by first intention. It has been the author's observation that more vision has been lost in chemical burns due to focal infection than by the actual effect of the offending agent.

Aftercare of the denuded eye

This subject is of utmost importance

and careful attention to detail will be rewarded with satisfactory results. Warning is given the patient at the first consultation that considerable pain is to be expected, due to the denuding, and each patient is provided with 0.5-percent ophthalmic pontocaine ointment, with instructions to apply it aseptically to the eye as frequently as is needed to control pain. Some persons, due to a difference in pain threshold, will require barbiturates, and a few may need morphine. The immobilizing patch is to be worn at all times except during actual treatment.

The eyes are inspected under fluorescein stain upon the day following denudation and, if found to be healing by first intention, no change is made in therapy. If, however, undue reaction is found, the eye is placed at temporary rest by the instillation of a few drops of 5-percent homatropine solution, and 5-percent sulfathiazole ointment is added at four-hour intervals. The choice of homatropine is made so that loss of time, an important factor in industrial practice, will be minimized if the eye heals promptly.

On the third day, inspection is again made, and, if healing is not complete, there is presumptive evidence that the burn has converted to an infected ulcer, and active combative treatment is instituted. The eye itself is sprinkled with methylene-blue powder, and the excess flushed away. Pontocaine, sulfathiazole, and the immobilizing patch are continued. An intramuscular injection of 5 c.c. of proteolac (G. D. Searle and Company) is given, and administration of maximum doses of sodium salicylate is started. Dental X-ray or medical examination of other foci is made, and such areas, if amenable to treatment, are removed at the earliest possible moment, regardless of the condition of the eye. In the event that surgical treatment of foci is to be undertaken, the patient is hospitalized and intravenous typhoid-vaccine fever therapy is begun. The surgical procedures are so arranged that they fall on the rest day in the typhoid series. At this point, the eye is atropinized because prevention of time loss is no longer a factor to be considered, and the whole attention must be turned toward the healing of the eye.

After healing has taken place and the cornea has been free from fluorescein staining areas for 48 hours, any residual opacity is treated with increasing percentages of dionin or with choline chloride.

Case reports

Table 2 lists 500 consecutive cases of chemical eye burn treated by the author in the last three years. Details of the seven cases in which some loss of vision resulted follow this table.

Due to the fact that they were in the process of manufacture, the chemicals listed varied in concentration and purity. Many of them are recorded by the abbreviated names under which they are known in industry, and many are actually combinations of several substances which are used in the manufacture of a given product. While the author realizes that inaccuracies exist, it is, nevertheless, significant that the denuding technique is efficacious upon burns from a wide variety of chemicals.

Cases of loss of vision

Case 1. Acetic-anhydride burn. This case was treated with the proper technique but the patient had several abscessed teeth and was very uncoöperative, refusing to remain in the hospital. The teeth were finally extracted on the second admission to the hospital but irreparable damage to the eye had taken place. Total loss of vision of the injured eye resulted. Notable in this case is the fact that another employee was injured as severely in the same accident. He was

TABLE 2

CHEMICALS WHICH PRODUCED 500 HUMAN CORNEAL BURNS, AND THE RESULTS OF TREATMENT BY THE DENUDING TECHNIQUE

Chemical	Prompt Healing 48 Hours	Slow Healing 3–10 Days	Loss of Vision
"Absorbine Jr."	—	1	—
Acetaldehyde	30	3	—
Acetic anhydride	16	3	1
Acetoacetanalide	2	1	—
Acetone	3	—	—
Acetyl chloride	1	—	—
Acetylene tetrachloride	1	—	—
Acrolein	1	—	—
Alkylized tin	—	1	—
Allyl alcohol	5	1	—
Alum	2	—	—
Aluminum chloride	4	1	—
Aluminum nitrate	1	—	—
Aluminum sulphate	1	—	—
Ammonia, aqueous	3	—	—
Ammonia, anhydrous	1	—	—
Benzene	3	—	—
Benzoic acid+phenylmethyl ketone	1	—	—
Butadiene	2	—	—
Butyl acetate	1	—	—
Butyraldehyde	6	—	—
Butanol	1	—	—
Calcium carbide	3	—	—
Calcium carbonate	1	—	—
"Carbic" anhydride	3	—	—
Catechol	4	2	—
"Catalyst gel"	1	—	—
"Cellosolve," methyl	1	—	—
Dichlorethyl ether	1	—	—
"Clorox" bleach	1	—	—
Cresylic acid	1	—	—
Crotonaldehyde	8	—	—
Dibutyl methiolate	1	—	—
Diethylethanolamine	1	—	—
Diketene	2	—	—
Dimethyl phthalate	1	—	—
Diphenyl oxide	4	—	—
"Drano"	—	—	1
"Dripolene"	1	—	—
Ethanol	1	—	—
Ethyl benzene	3	—	—
Ethylhexanoic acid	1	—	—
Ethylene chlorhydrin	4	—	—
Ethylene dichloride	20	—	—
Ethylene oxide	1	—	—
Ethanol toluene azetrope	1	—	—
Hexanol	4	—	—
Hexachlorethane	1	—	—
Hexaethyl benzene	1	—	—
Hydrofluoric acid	2	—	—
Hydrogen sulfide	6	—	—
Isophorone	1	—	—
Isopropyl acetate	—	2	—
Isopropanol	2	—	—
Lime	51	3	3
Lye (household)	1	—	1
"Magic Washer" (household bleach)	1	—	—
Maleic anhydride	14	—	—
Methanol+ethylene dichloride	2	—	—
Methyl chloride	1	—	—
Monoethanolamine	3	—	—
Naphtha	1	—	—
"Nickel catalyst"	8	1	—
"Oakite"	1	—	—
Octyl alcohol	2	—	—
Oxalic acid	2	—	—
Phenylmethyl carbinol	2	—	—
Phenylmethyl carbinol +Phenylmethyl ketone	1	1	—
Phosphorous oxychloride	1	1	—
Phthalic anhydride	8	—	—
Potassium dichromate	1	—	—
Potassium hydroxide, 50%	1	—	—
Potassium persulphate	1	—	—
Propylene oxide	3	—	—
"Silver catalyst"	1	—	—
Silver nitrate 50%	—	1	—
Soap powder	1	—	—
Soda ash	1	—	—
Sodium hydroxide (solid)	12	2	—
Sodium hydroxide, over 50%	—	2	—
Sodium hydroxide, 26 to 50%	27	1	1
Sodium hydroxide, 10 to 25%	89	3	—
Styrene	29	1	—
Sodium sulphide	5	2	—
Sorbic acid	1	—	—
Tantalum fluoride	1	—	—
Toluene	2	—	—
Trichloroethane	1	—	—
Vinyl acetate	1	—	—
Vinyl chloride	1	—	—
Vinyl ethyl ether	1	—	—
Viscose	—	1	—
Unknowns, various	13	3	—
Totals	458	37	7

given identical treatment, and healing was by first intention.

Case 2. Fifty-percent sodium-hydroxide burn. This case was not seen by the author for 48 hours after the burn. On first examination, it was determined that Bowman's membrane was involved, and a poor prognosis was given at that

time. The final vision in this case was 20/50.

Case 3. Lime burn. The patient in this case was treated by a general practitioner for three days previous to the time he was seen by the author. At that time, damage had already resulted. The patient was in poor health, having several infected teeth. After a protracted convalescence, the final vision in the injured eye was 20/60.

Case 4. Lime burn. This case was first seen by the author four days after the injury and no treatment of any kind had been given the patient. General health was poor, and loss of vision in the injured eye was total.

Case 5. Lime burn. The patient was given no first aid but was seen by the author within three hours after the injury. Healing was by first intention, but the newly formed epithelium broke down on the seventh day. Several abscessed teeth were removed on the same day, but a residual scar resulted. Final vision in the injured eye was 20/25.

Case 6. Fifty-percent sodium-hydroxide burn. The patient was not given the usual first-aid therapy and was not seen by the author until 24 hours after the injury. His general health was good. Final vision in the injured eye was 20/25.

Case 7. Twenty-five percent sodium-hydroxide burn. This case was treated according to the routine, but the patient had many broken and abscessed teeth and was in poor health. The final vision in the injured eye was 20/30.

Summary

From the study of 500 consecutive cases, the following conclusions are drawn:

1. Immediate first aid, followed by long flushing with water is of the utmost importance. No attempt at neutralization is recommended.

2. Specialized treatment by an ophthalmologist should be given within two hours after the injury. Further delay threatens recovery of full vision.

3. Denudation is the treatment of choice.

4. It is noted that the majority of cases, 456, or 91.2 percent, healed in 48 hours with no loss of vision; 37, or 7.4 percent, healed slowly, but without loss of vision; 7 cases, or 1.4 percent, healed with a residual loss of vision. The loss of vision in all seven cases was the result of inadequate preliminary care or health conditions present before the eyes were burned.

5. There is no mention made of conjunctival adhesions in this discussion, and it is notable that with the technique described the author had no such complication in any of these 500 consecutive cases.

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CHEMICAL BURNS OF THE RABBIT CORNEA*

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One of the most frequent and disturbing injuries that may occur in the manufacture of chemicals is accidental introduction into the eye. If time lost as a result of the accident is to be minimized, and impairment or loss of vision prevented, coördinated effort on the part of the plant medical service, the ophthalmologist, and the laboratory investigating plant hazards is essential. The clinical phases of this effort are discussed by McLaughlin[1] upon adjoining pages of this Journal. Where the behavior of the offending agent introduced into the eye has been determined by experiment upon animals, a better estimate of the potential seriousness of the injury may be made, and a more rational therapy instituted.

ESTIMATION OF EYE HAZARD BY THE RANGE-FINDING TEST

We have described elsewhere a quantitative method of assay to delineate the ability of a material to cause chemical burns of the rabbit eye as part of our range-finding test.[2] Because of the frequency of accidental entry of fluids into the eye, it was thought worthwhile to grade the severity of eye burns resulting from a large number of chemicals and mixtures. The work was started in 1938, and more than 4,000 rabbit eyes have been used to obtain this information.

We standardized the test for our own use six years before the communication of Friedenwald, Hughes, and Hermann[3] was published, but it has been possible to employ a scheme not unlike theirs to translate each injury into a numerical score. The system is shown in table 1.

The validity of this procedure is established by the fact that, in those eyes in which we have followed healing, the time required for repair and the area of any terminal corneal scar were roughly proportional to the numerical score assigned to the initial injury. Moreover, the scores for injuries caused by decreasing volumes or decreasing concentrations of a chemical form a smoothly descending numerical series.

TABLE 1

SYSTEM FOR NUMERICAL SCORING OF INJURY TO THE RABBIT EYE 24 HOURS AFTER APPLICATION OF A MATERIAL

	Points	Maximum
Symptom Visible Before Fluorescein Staining		
Cornea dull	2	
Cornea opaque, less than half of area	4	
Cornea opaque, more than half of area	6	6
Keratoconus		6
Iritis, slight internal congestion	1	
Iritis, marked internal congestion	2	2
Symptom Visible After Fluorescein Staining (If necrosis is diffuse assign points corresponding to half observed area)		
Necrosis on less than 5% of cornea	1	
Necrosis on 5 to 12%	2	
Necrosis on 13 to 37%	3	
Necrosis on 38 to 62%	4	
Necrosis on 63 to 87%	5	
Necrosis on 88 to 100%	6	6
Total		20

The individual numerical scores of each eye treated with a given volume or concentration of a chemical are added together and then divided by the number of eyes (usually 5) to obtain the score of the injury caused by the treatment. We

*From the Mellon Institute.

have selected a level of 5.0 as representative of severe injury. This figure corresponds to necrosis, visible only after staining and covering about three fourths of the surface of the cornea; or a more severe necrosis covering a smaller area.

When a test is to be performed, normal albino rabbit eyes are selected on the basis of absence of grossly visible staining by a 5-percent aqueous solution of fluorescein sodium, flushed with distilled water 20 seconds after application. After a two-hour interval to allow the eye to return to normal, 0.005 ml. of the undiluted material is applied to the center of the cornea while the lids are retracted. About one minute later, the lids are released. This procedure is necessary to prevent the removal of a portion of the dose by the very efficient wiping system of the lids before intimate contact has been made with the eye. Eighteen to 24 hours later, the eye is examined in strong diffuse daylight, then stained with fluorescein, and the injury scored. Guided by the result and the table of injury grades below, additional applications are made until the chemical can be assigned to one of the grades we recognize. If large volumes are applied, the lids are held closed for one minute before the animal is released.

Where dilution of a chemical is necessary, our preferred solvent is propylene glycol from a batch shown to cause no injury. Preference is next given to water, and in some cases a deordorized kerosene known as "Deobase" has been used.

Our grading system is set forth in table 2. No ambiguities have yet been found, although they might be expected in a system that depends partly on volume and partly on concentration. The combination is necessary to separate the damage produced by chemicals of obviously diverse abilities to injure that cannot be distinguished on the basis of the reaction to 0.005 ml. undiluted.

TABLE 2

GRADES OF INJURY EMPLOYED FOR RATING THE RELATIVE DAMAGE PRODUCED BY CHEMICALS IN THE EYE

Injury Grade	Definition
1.	0.5 ml. undiluted gives injury of 0 to 1.0 points
2.	0.5 ml. undiluted gives injury of over 1.0 up to 5.0 points
3.	0.1 ml. undiluted gives injury of up to 5.0 points (0.5 ml. gives over 5.0)
4.	0.02 ml. undiluted gives injury of up to 5.0 points (0.1 ml. gives over 5.0)
5.	0.005 ml. undiluted gives injury of up to 5.0 points (0.02 ml. gives over 5.0)
6.	Excess of 40% solution gives injury of up to 5.0 points (0.005 ml. gives over 5.0)
7.	Excess of 15% solution gives injury of up to 5.0 points (40% gives over 5.0)
8.	Excess of 5% solution gives injury of up to 5.0 points (15% gives over 5.0)
9.	Excess of 1% solution gives injury of up to 5.0 points (5% gives over 5.0)
10.	Excess of 1% solution gives injury of over 5.0 points

A total of 180 chemicals arranged according to the injury grades in which they fall appears in table 3. It must be recognized that in many cases somewhat impure industrial products have been tested, and impurities may possibly place some compounds in a grade other than that which would be occupied by a pure preparation. An asterisk (*) marks chemicals known to have caused loss of vision or very slowly healing corneal burns in industrial use, exclusive of injury produced only by vapors, which is a quite separate problem. It will be seen that the asterisks are associated with the higher grades. It must be recognized that a viscous chemical is less likely to reach the eye than is a more mobile compound and, accordingly, the grades here defined do not reveal the true hazard of handling the compounds, but rather their relative potential ability to cause damage once they reach the eye.

As related by McLaughlin,[1] the lists have been used with profit by one industrial medical service for prediction of the probability of permanent injury in a particular accident and for indication in the plant dispensary of the therapeutic measures that are to be followed. Although these lists have been found useful and fairly reliable in practice, there have been a few instances in which they have

TABLE 3

INJURY GRADES OF SOME CHEMICALS WHEN APPLIED TO THE RABBIT EYE

Grade 1 (0.5 ml. undiluted yields score of 0 to 1.0)

Butyl phthalyl butyl glycolate
1-3 Butylene glycol
"Carbowax" compound 1,500
"Carbowax" compound 4,000
Castor oil
Deobase (deodorized kerosene)
Diallyl phthalate
Dibutyl "Cellosolve" phthalate
Di-2-chlorethyl formal
Dicyanoethyl sulfide
Di-2-ethylhexyl phthalate
Diethylene glycol
Di-isobutyl ketone
Dimethoxy tetraglycol
Dimethyl tetrahydrophthalate
Dipropylene glycol
Ethoxy triglycol
2-Ethylhexyl acetate
Ethylene glycol
Ethylene glycol diacetate
Glycerine
Hexaethylene glycol
Methyl acetyl ricinoleate
Methyl "Carbitol" formal
Methyl "Cellosolve" acetyl ricinoleate
Methyl phthalyl ethyl glycolate
Methyl styryl phenyl ketone
Nonaethylene glycol
Polyethylene glycols 200, 300, 400, 600
Polypropylene glycol
Propylene glycol
Tetradecanol
Tetraethylene glycol
Tri-2-ethylhexyl phosphate
Triethylene glycol
Tri-isopropyl phenyl phosphate

Grade 2 (0.5 ml. undiluted yields score of over 1.0 and not over 5.0)

Allyl chloride
Butyl "Carbitol" acetate
"Carbitol"
"Carbitol" acetate
Chlorethyl benzene
Dibutyl "Cellosolve" succinate
Diethylene glycol diacetate
Dimethyl "Carbate"
Dimethyl phthalate
2-Ethylhexyl-2-ethylhexanoate
Ethylene cyanohydrin
Isopropenyl acetate
Methyl borate (96% ester)
Methyl "Carbitol"
Methyl "Cellosolve" acetate
Paraffin oil U.S.P.
Propylene glycol diacetate
Pyruvic aldehyde
Thiodiethylene glycol
Tributyl phosphite

Grade 3 (0.5 ml. undiluted yields score of over 5.0 and 0.1 ml. yields not over 5.0)

"Cellosolve"
"Cellosolve" acetate
Diallyl maleate
Dicyanoethyl amine
Diethyl "Carbitol"
Dimethyl maleate
Ethanol
Ethyl benzene
Ethyl propyl acrolein
Ethylene dichloride
Hydroxyethyl acetamide
Methanol
Undecanol
Tributyl phosphate
Oil of citronella
Methyl salicylate
Methyl benzyl "Cellosolve"
Methyl "Cellosolve"

Grade 4 (0.1 ml. yields score of over 5.0 and 0.02 ml. yields not over 5.0)

Acetonyl acetone
Butyl "Cellosolve"
3-Chloropropane diol-1,2
Dichlorethyl ether
Diethyl "Cellosolve"
Dioxane
Epichlorhydrin
Ethyl acetoacetate
Ethyl ether of propylene glycol
Ethylene glycol monacetate
Ethylene sulfide
Formamide
Isophorone
Isopropanol
Methyl acrylate
Methyl "Carbitol" acetate
Methyl ether of propylene glycol
Propylene oxide tetramer
*Styrene
Tetrahydrodimethyl furane
Triethylene glycol dichloride
Trimethyl cyclohexanone

Grade 5 (0.02 ml. yields score of over 5.0 and 0.005 ml. yields not over 5.0)

Acetol
Acetone
*Allyl alcohol
Butyl "Carbitol"
Cyclohexanone
Diacetone alcohol
2,3-dichloropropanol-1
Diethanolamine
Diethyl sulfate
Diethylene triamine
Diglycol chlorhydrin
Dimethyl dioxane
Dimethyl furane
Dioctyl tetrahydrophthalate
Ethyl borate
Ethyl crotonate
Ethyl hexane diol
2-Ethyl hexanoic anhydride
2-Ethyl hexanol
2-Ethyl hexoic acid
Ethyl mandelate
Ethylene glycol diformate
Glyoxal (32.8% technical)
Hydroxyethylene diamine
Isobutanol
Isopropyl mandelate
Isopropyl oil
Mesityl oxide
Methyl diacetoacetate
Methyl-3-hydroxybutyrate
n-Morpholine ethanol
Methyl dioxolane
Pentane dione
Phenyl ethanolamine
Propylene oxide
Soap, USP tincture green
Triethanolamine
Tetraethanol ammonium hydroxide (40%)

Grade 6 (0.005 ml. yields score of over 5.0, excess of 40% solution not over 5.0)

Dibutoxy tetraglycol
2-Ethylhexyl acrylate
Tri-isopropanolamine

Grade 7 (0.005 ml. and 40% solution yield scores of over 5.0, 15% solution not over 5.0)

n-Butanol
Benzyl "Cellosolve"
Cyclohexanol
*Ethylene chlorhydrin
*Ethylene imine
Glycolic acid
Isopropanolamines, mixed
Mercaptoethanol
Methyl acetoacetate
Morpholine
Phenyl methyl carbinol
Propylene chlorhydrin
Toluene

Grade 8 (0.005 ml. and 15% solution yield scores of over 5.0, 5% solution not over 5.0)

Caproic acid
*Di-2-ethylhexyl amine
Di-n-Hexyl amine
*Dimethyl sulfate
*Ethylene diamine
*Formaldehyde
Lactic acid
Phenyl methyl ketone
Soap (granulated white)
Succinic acid
Succinic anhydride
Tetramethyl ethylene diamine
Trimethyl adipic acid

Grade 9 (0.005 ml. and 5% solution yield scores of over 5.0, 1% solution not over 5.0)

*Acetic anhydride
*Ammonium hydroxide
*Ethyl chloracetate
2-Heptadecyl imidazoline
Menthol
*Methyl silicate
Monoethanolamine
Piperazine
*Propylene imine
*Sulfuric acid
Tributyl phosphine oxide
Trimethyl cyclohexanol
3,5-Xylenol

Grade 10 (1% solution yields score of over 5.0)

*Maleic anhydride
*Sodium hydroxide

* Compounds known to have caused severe human eye injury.

resulted in misleading prognoses regarding particular eye burns. These difficulties can be attributed largely to the fact that workmen are unable to inform the plant dispensary fully about the composition of fluids which they handle. There is also uncertainty of the relative sensitivity of human and rabbit eyes.

In general, only materials are included whose chemical names can be given. It is of some interest to relate that three commercial shampoos have been found

to fall in grades 4 and 5, and that those synthetic detergents which were tested fall in grades 5 to 8.

Neutralization of Alkali and Acid Burns

Although it might be expected that acid or alkali burns of the eye could be treated effectively by immediate neutralization, such has not proved to be the case with experimental burns of rabbit eyes. Both eyes of a rabbit were burned with acetic anhydride and flushed with water. One eye was then treated with milk of magnesia while the other served as a control. Repeated trials revealed no reduction in healing time nor any appreciable decrease in the severity of the burns. Actually, in some cases the injury was aggravated. This finding led to an investigation of the reaction produced by milk of magnesia on the normal rabbit eye. Four popular brands of the preparation were procured and 0.5-ml. amounts were instilled morning and afternoon daily. The eyes were stained each day with 5-percent fluorescein sodium, which by test had been found to cause no damage in itself upon repeated application. On the third or fourth day of treatment, necrosis involving 40 percent or more of the cornea resulted from instillation of two of four samples. This effect persisted while the daily administration of milk of magnesia continued. It required three to four days for the eyes to attain a normal condition after cessation of the doses. This irritative action was produced mechanically, it is believed, by brucite, a crystalline form of magnesium hydroxide, which appears in the amorphous product after storage.

The use of 2-percent citric acid as a flushing agent in the treatment of alkali burns of the eye has been proposed by Ridley.[4] To investigate the efficacy of this treatment, corneal burns were produced on both eyes of an anesthetized rabbit with 0.2 ml. of 0.5-percent sodium hydroxide, and the eyes were irrigated with 2-percent citric acid and 0.85-percent saline, respectively, for a 30-minute interval. At the end of this period, the anterior portion of the conjunctiva of the eye washed with citric acid had a coagulated appearance with extreme congestion and edema elsewhere. With slit-lamp observation, the lens was barely visible through the corneal opacity. The saline-treated eye had a congested conjunctiva, and the corneal opacity was about one half as dense as that of the other eye. Both eyes revealed complete surface necrosis upon staining with fluorescein the following day. The eye washed with citric acid showed opacity of the endothelium and Descemet's membrane with a cloudy stroma, whereas those structures were less injured than was the epithelium in the saline-treated eye. On the fifth day, the eye washed with citric acid had a thickened cornea, feathery opacity of the epithelium and stroma, and opacity of the endothelium. Macroscopically the opacity was very pronounced, and fluorescein stained the surface completely. At this time, the saline-washed eye was normal, with no opacity nor surface necrosis. After 17 days, the citric-acid-treated cornea contained a 3- by 3-mm. area filled with fluid in which were seen many punctate bodies, in all probability a leucocytic infiltration. There was considerable vascularization of the paralimbal region, and diffuse fluorescein staining of the cornea. After one month, this eye bore no resemblance to a functional organ because of necrosis, fibrosis, and conjunctival evagination.

To evaluate the effect of irrigation with 2-percent and 0.5-percent citric acid alone, normal unburned eyes of rabbits

under anesthesia were used. After 30 minutes, the left eye which received 2-percent citric acid had a cloudy cornea and edematous lids. The right eye, washed with 0.5-percent acid, had the same type of injury to a lesser degree. The opacity was localized in the internal layers of the cornea, either deep in the stroma or in Descemet's membrane and the endothelium. Twenty-four hours after the irrigation the left eye showed solid opacity and 100-percent necrosis with fluorescein. The right eye was cloudy and 80 percent of the cornea stained. After two weeks, the left eye was opaque, with a thickened cornea. The surface had 10-percent dense necrosis surrounded by opacity over the pupillary area, with some vascularization from the dorsal limbus. The stroma of the right eye was clearing nicely, but opacity of deeper layers was still visible under slitlamp observation. After the lapse of almost a month, there was a 5-mm. staphyloma over the pupillary area, which ruptured while the rabbit eye was being examined. The right eye showed cloudiness throughout the cornea under the slitlamp, an opacity that was also visible without aid.

Obviously, even though a single instillation of 0.5 ml. of 2-percent citric acid produced corneal necrosis in only one of five rabbit eyes, and applications repeated for seven days produced only sporadic nonpersisting small areas of necrosis, the 2-percent solution is absolutely and unequivocally to be avoided for prolonged irrigation. The same is true for 0.5-percent citric acid as an irrigating agent.

Qualitative studies on alkali burns

The remarkable healing of alkali burns of the human eye which had been treated by simple denudation led McLaughlin[1] to inquire into the mechanism of action underlying the necessity for complete removal of the affected tissue as a means of preventing penetration and subsequent damage to the eye. A request for collaboration in the investigation of these problems was made to us.

The first matter for consideration was the suitability of the eye of the albino rabbit for test purposes. Walls[5] states that a Bowman's membrane is seldom discriminable in the placentalian eye and in lower animals cannot ordinarily be discerned as a distinct part of the substantia propria. Our inability to measure the thickness of Bowman's membrane in the living animal by means of the slitlamp led us to the examination of stained histologic preparations, as differences in structural dimensions between the human and rabbit cornea might well have an important bearing on their respective responses to treatment after chemical burns.

Stained histologic sections of normal human and rabbit corneas were measured microscopically. The human corneal epithelium and Bowman's membrane measure 45.4 and 8.4 microns, respectively, compared to 33.6 and 1.75 microns for the corresponding structures in the rabbit eye. Although these figures do not represent *in vivo* dimensions, they illustrate the relative differences. The greater thickness of the epithelium of the human cornea presents a better mechanical barrier to chemicals penetrating to Bowman's membrane. Furthermore, this thicker epithelium of the human eye will permit deeper denudation for the removal of the offending agent without damage to the underlying Bowman's membrane, the integrity of which must be preserved if scar formation is to be prevented. This quantitative difference in structure may offer a decided advantage to the ophthalmologist in treating human-eye burns by the denudation technique. (The foregoing refers to a structure discriminable in

stained preparations, which we interpret as Bowman's membrane.)

Eye injuries produced by chemicals may be divided into three categories; namely, those produced by neutral, acid, and alkaline materials. Acid causes an immediate reaction which does not appear to increase in depth with time. Neutral chemicals usually act similarly, but some cause delayed burns. For example, the history in a few human cases which we observed could be explained only on the basis of a delay of several hours between contact with a fluid ester (methyl silicate) and development of injury. The mechanism causing a delay is not yet clarified. Acid and neutral burns were not investigated in the present study. Following alkali burns, McLaughlin[1] found, clinically, that immediate denudation of the involved area becomes necessary to prompt healing, presumably because it prevents penetration of alkali into Bowman's membrane. This fact raises the question as to what may happen after alkali reaches the eye. The damage may be caused by the lytic action of the alkali *per se*, by a product formed as a result of its chemical union with protein, or possibly by the elaboration of some agent from injured cells which stimulates the inflammatory process.[6]

The presence of alkali retained after flushing was demonstrated by the use of an ordinary pH indicator. Rabbits were anesthetized, and 0.05- to 1.0-ml. amounts of aqueous 4-percent sodium hydroxide were pipetted onto the cornea and allowed to remain for 30 seconds. Irrigation or continuous surface flushing of the eye with 0.85-percent sodium chloride was then instituted and continued for 30 minutes. Retention of hydroxyl ions was determined by excising a 2- or 3-mm. circle of corneal epithelium and testing its reaction. The tissue was at once mounted in a sealed hanging-drop preparation in unbuffered 0.03-percent metacresol-purple indicator adjusted to the midpoint of its range, which covers pH 7.6 to 9.2. This indicator was selected because its range is above pH 7.2, the reaction of the normal surface of the rabbit cornea. Similar pieces of corneal tissue were always taken from the unburned eye of the same rabbit to serve as controls. Numerous trials with such preparations demonstrated that normal corneal epithelium was acid to the indicator, as it produced a yellow color, whereas tissue from the alkali-burned eye was strongly basic as evidenced by the development of a purple color. Furthermore, when a series of rabbits were treated and killed singly at various intervals of time, traces of alkali could be demonstrated, colorimetrically, 24 hours following the application and flushing.

The pH of the normal and alkali-burned corneas was also determined electrometrically with a glass electrode shaped to fit the curvature of the eyeball. Eyes were burned with 0.2 ml. of 1.0-percent sodium hydroxide and also with the same amount of a 5-percent aqueous solution of a less highly ionized alkali, ethylene diamine. All burned eyes were irrigated with physiologic saline for 30 minutes before the surface pH was determined. The left eye of each rabbit was burned, and the right eye served as a control.

The figures given in table 4 are in-

TABLE 4

ELECTROMETRIC pH DETERMINATIONS OF BURNED AND NORMAL RABBIT EYES, AFTER 30-MINUTES' FLUSHING

	NaOH	Ethylene Diamine
Surface pH of burned left eye	8.0	8.1
Surface pH of normal right eye	7.2	7.2
Aqueous humor of burned left eye	8.5	8.7
Aqueous humor of normal right eye	8.2	8.2

teresting in that the normal pH of aqueous humor of the human eye according to Best and Taylor[7] is 7.1 to 7.3, whereas the determinations on normal rabbit aqueous humor indicate a pH of 8.2, or 10 times the hydroxyl-ion concentration of the human aqueous. The demonstration of increased alkalinity of the aqueous humor following sodium-hydroxide and ethylene-diamine burns illustrates the ability of alkaline materials to penetrate the rabbit cornea. It would be expected, therefore, that where the buffering capacity of the aqueous humor is exceeded, damage to delicate internal structures of the eye will occur.

An *in vivo* test was devised to verify further the presence of alkali in tissue burned with sodium hydroxide. This technique is referred to as a "transfer burn" for reasons which the procedure will make plain.

After intravenous sodium-pentobarbitol anesthesia, one eye of the first rabbit, the transfer donor, is burned with 0.2 ml. of 1-percent sodium hydroxide and irrigated for 30 minutes with 0.85-percent sodium chloride, after which the animal is killed by intravenous air embolism. The superficial layers of the cornea—that is, epithelium and adherent substantia propria —are peeled from the entire anterior surface of the eye in one piece. This tissue is repeatedly punctured with the point of a scalpel and trimmed in the form of a cross. The perforation increases the opportunity for retained alkali to escape and the crosslike pattern provides tissue which will make good contact upon application to the normal eye of a second rabbit, the transfer recipient. Great care was exercised at all points to eliminate the possibility of alkali being carried by the instruments used.

The recipient is anesthetized and immobilized so that its head cannot be moved. The cross-shaped tissue from the donor is placed with its center over the pupillary area of the recipient so that the burned epithelium is in contact with the normal recipient epithelium. This piece of tissue is kept in place for a one-hour period, during which time the lids of the recipient are held apart in order that the tissue will not be disturbed nor tears flush the pupil. The transfer tissue is prevented from dehydration by the addition of 0.01-ml. amounts of distilled water as required.

After a one-hour contact period, the recipient is killed by air embolism, and the transfer tissue from the donor is removed and tested with meta-cresol-purple indicator to ascertain whether it still contains alkali. A 5- by 5-mm. piece of recipient corneal tissue which has been in intimate contact with donor tissue is then peeled off and likewise tested with the indicator in a sealed hanging-drop preparation. Repeated trials with this method resulted in the colorimetric demonstration of alkali in or upon the recipient corneal epithelium when tissue was taken from over the pupillary area where contact with the donor tissue had been most intimate. The colorimetric demonstration of alkali may fail if small pieces of corneal tissue about 1 by 2 mm. in size are removed and tested individually. This failure may be due to the fact that the alkali present in such a small piece of tissue is insufficient to cause a color change in the relatively large drop of indicator solution used, or that all portions of the recipient cornea are not uniformly burned with alkali. Roughly indentical pieces of corneal tissue removed from the untouched control eye of the recipient always produced a yellow color with the indicator, which denotes pH 7.6 or less, whereas the treated recipient cornea produced a purple color, indicating pH 8.2 or above. The indicator must be accurately adjusted to the midpoint of its

range or the minute amounts of alkali present in the recipient cornea may not be sufficient to effect the color change

To serve as a control on manipulative procedures, the test was carried out with the use of normal donor tissue instead of that burned by sodium hydroxide, but with entirely negative results. All tissue tested remained acid to the indicator. Earlier attempts at fluorescein staining of recipient cornea were abandoned as a means of detecting the presence of injury caused by the transfer of alkali when it was discovered that all rabbit eyes show a punctate staining of the cornea after 20 seconds' contact with 5-percent fluorescein under slitlamp observation, although macroscopically they were not visibly stained. This type of staining could not be demonstrated in normal human eyes when the same fluorescein stain was used. The recognition of this fact forced reliance upon indicator solutions for the demonstration, for the burns produced by the transfer method were so minute that direct slitlamp observations without fluorescein staining were not considered reliable. A further objection to the use of fluorescein at this point is that it would not distinguish between mechanical injury and chemical injury from alkali. On one occasion, a small opacity which persisted for 24 hours was noted, but the use of the indicator remained the method of choice. The presence of alkali was also demonstrated after the recipient's cornea was washed for about 5 seconds with distilled water before removal for testing with the indicator.

In view of the demonstration of increased hydroxyl-ion content of the aqueous humor following severe burns with sodium hydroxide, it was thought advisable to attempt a transfer burn by using aqueous humor taken from a burned eye. The procedure was essentially the same as has been described except that aqueous humor was aspirated by means of a syringe and 26-gauge needle from both the burned and normal donor eyes and was applied dropwise every 5 minutes for 1 hour to one eye on each of two recipients. This procedure resulted in the action of aqueous humor from the donor's burned eye being compared with that from the donor's normal eye which served as a control. Slitlamp observation of both recipients' eyes showed no visible damage. The eyes were then flooded with distilled water for 5 or 10 seconds to remove any of the aqueous humor adhering to the surface. Colorimetric tests revealed that portions of the cornea removed from these eyes after the animals were killed did not differ from their normal untreated eyes. This demonstration indicates the probable buffer action of the aqueous humor which had been shown by electrometric determinations to have an increased hydroxyl-ion content.

Denudation

The outstanding success accomplished by simple denudation of burned corneal tissue in the treatment of human eye burns is reported by McLaughlin.[1] The application of this technique to the treatment of controlled experimental burns of the rabbit cornea did not produce comparable results in our hands. It required three days for a normal rabbit eye to heal after it had been denuded by the cotton-swab method following the instillation of 4-percent cocaine hydrochloride. This interval is about three times as long as it required for the regeneration of human corneal epithelium. Numerous controlled experiments that compared denudation and no treatment led to the conclusion that in dealing with the rabbit cornea any mechanical interference will retard rather than foster the natural healing process. Despite the quantitative differences in

structure previously mentioned, observation has shown that the rabbit eye has enormous regenerative power following very severe damage and that injury to Bowman's membrane does not always result in scar-tissue formation as is the accepted fact in the case of burns of the human eye although it now appears that its corneal epithelium regenerates slowly.

Although species difference prevented the confirmation of McLaughlin's findings when using the rabbit eye, his consistently successful results amply justify his recommended therapy.

Conclusions

Experiments have been made upon corneal burns in the rabbit intended to assist in the therapy of human corneal burns in industry. The results of this work point to certain conclusions.

1. It is possible to grade the ability of fluid and dissolved chemicals to injure the cornea on the basis of application of a series of volumes and concentrations to the rabbit eye. The results correlate well with clinical experience in a plant handling a wide variety of compounds.

2. Alkaline molecules reaching the cornea are bound in some fashion to the epithelial cells and are not removed by prolonged washing with saline or water. Alkali bound in this fashion will be liberated from excised epithelium to injure intact epithelium in contact with the former. Presumably alkali is slowly liberated from its original site of fixation in the living eye to injure neighboring cells and result in a progressive burn.

3. Attempts to neutralize alkali on the cornea by prolonged flushing with dilute citric-acid solutions result in seriously aggravating the condition of the eye. Similar attempts to neutralize acetic-anhydride burns with milk-of-magnesia applications are less spectacularly harmful but they are not beneficial.

4. Alkali contacting the cornea penetrates it to a sufficient extent to raise the pH of the aqueous humor and threaten internal ocular structures.

5. The treatment of alkali burns upon rabbit cornea by denudation failed to demonstrate its effectiveness owing apparently to species differences in the rate of epithelial regeneration.

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FURTHER OBSERVATIONS ON AQUEOUS VEINS*

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Although the site of exit of the intraocular fluid has been discussed for many decades, the actual elimination of the aqueous humor was biomicroscopically observed in May, 1941.[1] In, or beneath, the conjunctiva of normal human eyes, I chanced to see small, almost or completely colorless vessels emerging from the depth of the corneal limbus or from the limbal meshwork or from a scleral emissarium. When they joined episcleral or conjunctival veins, these clear vessels produced a more or less marked dilution of the blood streaming through these veins; often they continued to transmit a layer of clear fluid into the vein they had joined. I proposed to name these vessels, "aqueous veins," assuming that they were biomicroscopically visible pathways carrying intraocular fluid from Schlemm's canal and the deep scleral venous meshwork to the episcleral, conjunctival, and anterior ciliary veins.

Leaving the canal of Schlemm, the aqueous humor may rapidly and completely mix with the blood contained in the scleral venous meshwork (fig. 1), in which case, no clear fluid becomes visible in any of the conjunctival or subconjunctival veins. If and where, however, aqueous humor passes through the scleral meshwork without being mixed with blood, or accepting only a small amount of blood, clear fluid will become discernible (figs. 2, 3, 4). (See also table 1.)

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While many ophthalmologists have had difficulty in recognizing the aqueous veins, others have confirmed their occurrence and significance. Some of these confirmations came a short time after the discovery of the biomicroscopically visible intraocular-fluid elimination was published, some later.

Vail became familiar with the aqueous veins soon after their detection and emphasized their importance.[2] Troncoso[3] recognized the aqueous veins as an anatomic-physiologic fact. Verhoeff[4] was the first to raise the farsighted question as to whether, with high intraocular pressure and a normal filtration angle, the clear stream in the aqueous veins would become longer. This question could not be answered immediately. Further observations on glaucomatous eyes[5] showed that, in primary compensated glaucoma, the flow of aqueous is less vigorous and that it may become stronger after successful treatment with miotics or after successful surgery. Berliner[6] referred to the aqueous veins without espousing their cause; this may be explained by the fact that, according to his references, only the preliminary note about the aqueous veins was used and that a more extensive discussion[7] could not yet be considered for the manuscript of his textbook. Sugar[8] and Gartner[9] were able to see the aqueous veins, the latter even succeeded in photographing them. It is not easy to obtain satisfactory photographs of the aqueous veins proper, for they are only 0.01 to 0.1 mm. in diameter,[1, 10] and, since they are mostly colorless trails, contrast but little with the surrounding sclera. The recipient vessels, characterized by their stratification, are more easily observable by means of both

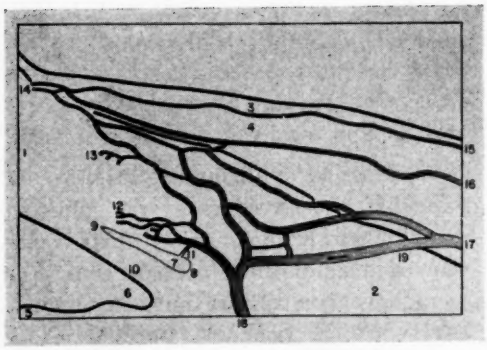

Fig. 1 (Ascher). AQUEOUS HUMOR LEAVING THE CANAL. Upon leaving the canal, the aqueous usually fades into the venous blood of the scleral meshwork. Therefore, no clear fluid is visible in the superficial veins of more than one half of all normal, quiet eyes.

Numerals on this diagram and those of illustrations 2 to 9 have the following significance: 1, Cornea. 2, Sclera. 3, Conjunctiva. 4, Subconjunctival space. 5, Iris. 6, Chamber angle. 7, Canal of Schlemm. 8, Scleral border of canal. 9, Corneal border of canal. 10, Trabecula. 11, Outlet of canal, falsely collector. 12, Venous part of deep meshwork. 13, Venous part of scleral meshwork. 14, Venous part of limbal meshwork. 15, Conjunctival vein. 16, Subconjunctival vein. 17, Anterior ciliary vein. 18, Anastomosis to ciliary body. 19, Emissarium sclerae. All arteries have been omitted for simplification.

biomicroscopy and photography.

Among those who have seen the aqueous veins but have not as yet published their observations, I should mention Kronfeld,[11] Rohner,[12] and Weve.[13]

Although I was able to see the aqueous veins in about every fourth, and later in every third eye of all normal eyes that came under my observation, Gartner[9] found them in 20 percent, and Goldmann[10] in 75 percent of persons examined. Most of the aqueous veins that I have seen were located in either eye between the 2- and the 4-o'clock positions or between the 8- and the 10-o'clock positions in, or at a short distance from, the corneoscleral limbus. Goldmann[10] found the aqueous veins mostly in the lower temporal or in the lower nasal quadrants. He, as well as Gartner,[9] confirmed the stratification or layering of aqueous and sanguineous fluid running in the same vessel and forming two or three or more parallel strata. Both observed changes of this stratification following experimental manipulations. Changes in the blood-aqueous ratio which occur in aqueous veins after compression (figs. 5, 6) of their recipient vessel (see ref. 1, p. 36; ref. 5, pp. 1077-1084; ref. 7, pp. 1193-1198) were confirmed by Sugar,[8] Gartner,[9] Goldmann,[10] and Kronfeld.[11] After compression of the recipient vessel, Goldmann more often observed an influx of

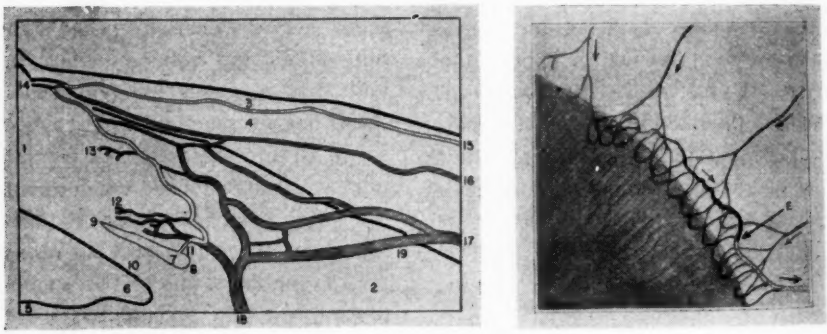

Fig. 2 (Ascher). Aqueous vein: ORIGIN IN LIMBAL LOOPS. *Diagram:* Having left the canal of Schlemm (7), clear fluid may pass the scleral meshwork (13) and, if not mixed with blood, may become visible in the limbal capillaries (14). *Drawing:* At the point E, the color of the vein abruptly changes to a very pale pink, proving the entrance of an aqueous vein from the depth of the limbus.

clear fluid (I had called this the positive glass-rod phenomenon), whereas Sugar[8] and Gartner[9] more frequently saw an influx of red blood cells into the aqueous backflow of blood into the canal of Schlemm. Goldmann[10] corroborated Sugar's conclusions, and mine, that the observations made on aqueous veins prove

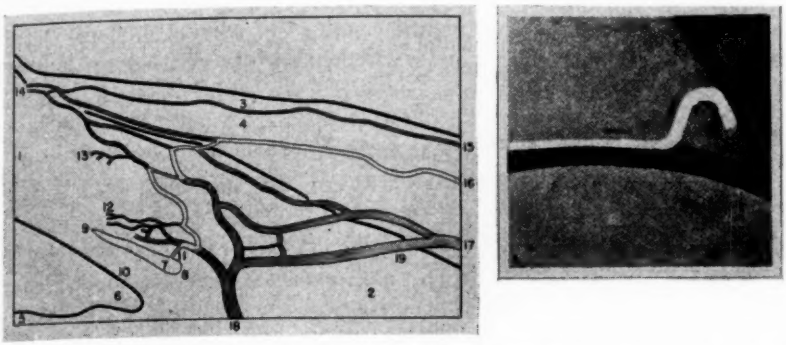

Fig. 3 (Ascher). Aqueous vein: ORIGIN IN SCLERAL TISSUE—the most common type of aqueous-vein origin. *Diagram:* Clear fluid, if not mixed with blood, may become visible in a spiral or U-shaped arch, one limb of which emerges out of the scleral tissue. *Drawing:* The peripheral limb of the U-shaped arch ascends into the conjunctiva to join a conjunctival vein and to form a stratified current.

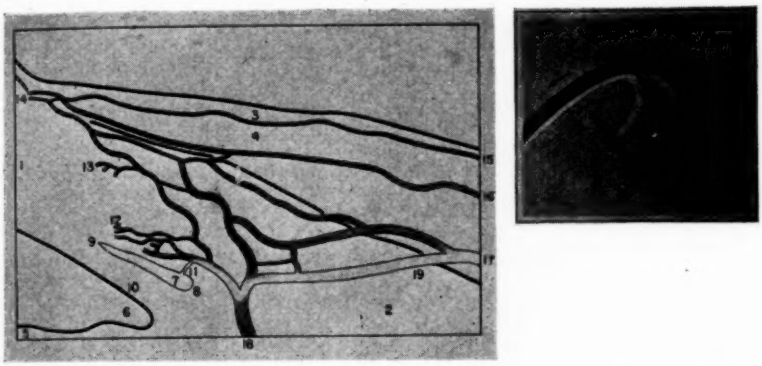

Fig. 4 (Ascher). Aqueous vein: ORIGIN FROM SCLERAL EMISSARIUM. *Diagram:* Having passed a part of the scleral meshwork, clear fluid may become visible in a scleral emissarium (19). *Drawing:* The largest aqueous veins are found among those originating from a scleral emissarium.

vein (the negative glass-rod phenomenon). Anatomic differences in individual eyes are, most probably, responsible for this apparent discrepancy (see ref. 5, p. 1084).

Sugar[14] expressed the opinion that the presence of the aqueous veins gives evidence for a through-and-through circulation of the aqueous humor, and that their presence also explains why the application of the gonioscopic contact lens may cause that there is a continuous elimination of aqueous humor taking place via the canal of Schlemm and the episcleral veins. Goldmann (ref. 10, p. 152) also agreed to my computation of the amount of aqueous humor eliminated by the aqueous veins. Considering the figures published about the diameters of the outlets of Schlemm's canal and those pertaining to the speed of movement in conjunctival vessels, I reached an approximate accord

between the amount of fluid possibly eliminated by aqueous veins and the estimations published in the literature (ref. 7, p. 1192).

Soon after the discovery of the aqueous veins, spontaneous as well as provoked pulsations were observed. These pulsations were synchronous with the radial pulse and consisted of minute changes in the position of border lines separating the aqueous and the sanguineous phases, respectively (see ref. 1, p. 36; ref. 7, pp. 1201-1203). Goldmann[10] confirmed the observation of these pulsating border lines and found that the peak of the clear-fluid influx was slightly delayed as compared to the radial pulse. He was able to increase these pulsations by instillation of adrenalin solution into the conjunctival sac.

Some of the pharmacologic effects which I have described[15] were confirmed by Gartner[9] and by Goldmann.[10] Gartner published photographs showing aqueous veins before and after administration of miotics. He confirmed my observation that miotics may markedly reduce the red-blood-cell content of an aqueous vein (see ref. 15, pp. 1302-1303; ref. 16, p. 1313). Goldmann[10] reported the effects of adrenalin administration on aqueous veins corresponding to my observations (ref. 15, pp. 1304-1306).

While Verhoeff[4] assumed a relationship between the increase of intraocular pressure and the visible outflow of aque-

TABLE 1

A PHYSIOLOGIC UNIT: THE CANAL OF SCHLEMM AND THE AQUEOUS VEINS

	Canal	Aqueous Veins
Embryology	Common primordial anlage (Sondermann, Ida Mann)*	Common primordial anlage
Anatomy	"Outer channels" connect Schlemm's canal with anterior ciliary veins (Schlemm, Leber, Maggiore, Troncoso, Henderson, Theobald, Friedenwald)	"Outer channels" connect Schlemm's canal with anterior ciliary veins
Physiology	Elimination of aqueous humor (Leber, Lauber, Troncoso, Seidel, Friedenwald)	Elimination of aqueous humor
Contents	Aqueous humor mixed with blood in varying proportions (Trantas, Salzmann, Troncoso, Friedenwald)	Aqueous humor mixed with blood in varying proportions
Distribution of contents	Stratification may occur (Troncoso)	Stratification very common
Changes in blood—aqueous ratio	Very common (Sugar, Bangerter & Goldmann, Kronfeld)	Very common
A. With increase of venous pressure	Backflow of blood into the canal (Bangerter & Goldmann)	Negative glass-rod phenomenon; i.e., blood enters the aqueous veins
B. With increase of aqueous pressure	Expulsion of blood from the canal (Kronfeld)	Positive glass-rod phenomenon; i.e., expulsion of blood from the aqueous veins
C. With decrease of aqueous pressure	Backflow of blood into the canal (Barkan, Kronfeld)	Negative glass-rod phenomenon; i.e., blood enters the aqueous veins

* For references quoted in this table see previous publications. [1,5,7]

ous humor, Gartner[9] expressed the opinion that damage to an aqueous vein during an operation for glaucoma might have considerable influence on the intraocular pressure. Therefore, he determined to locate the aqueous veins of glaucoma patients in order to avoid injuring these important structures during surgery. 1075-1077 and 1079-1087; ref. 16, pp. 1309-1314) a working hypothesis was evolved, an hypotheses which, it is to be hoped, may be confirmed by future histologic investigations. I assumed that transient or permanent narrowing in the outlets of Schlemm's canal may be the cause for the failure of glaucomatous eyes

TABLE 2

A UNIT OF CLINICAL SIGNIFICANCE: THE CANAL OF SCHLEMM AND THE AQUEOUS VEINS

Condition	Gonioscopy of the Canal Shows	Biomicroscopy of the Aqueous Veins Show
Inflammation	Blood enters the canal (Trantas, Salzmann, Koeppe, Troncoso)*	Aqueous veins filled with blood; therefore, not discernible
Congestion	Blood enters the canal (Schlemm)	Aqueous veins filled with blood; therefore, not discernible
Primary compensated glaucoma	Blood rarely enters the canal (Bangerter and Goldmann, Kronfeld). Wessely effect inverted	Negative glass-rod phenomenon; i.e., blood enters the aqueous vein after compression of the recipient vessel
Decompensated glaucoma	Not yet studied	Aqueous veins carry blood from posterior uvea; therefore, not discernible
Secondary glaucoma	Wessely effect present (John)	Mostly negative glass-rod phenomenon
Controlled glaucoma	Blood enters the canal (Kronfeld and assoc.)	Sometimes positive glass-rod phenomenon; i.e., clear fluid expells blood from aqueous vein after compression of the recipient vessel

*For references quoted in this table see previous publications. [1,5,7,16]

Because of the wide areas treated when operating by cyclodiathermy, the damage which this procedure might cause to the aqueous veins is of particular concern to Gartner. He advised that the aqueous veins be undisturbed during any operation for the relief of glaucoma. Goldmann[10] stressed the significance of the rapid outflow of aqueous humor, as observed biomicroscopically, for an understanding of the mechanism of such operations (table 2).

AQUEOUS VEINS IN THE ETIOLOGY AND CLASSIFICATION OF GLAUCOMA

From a cursory discussion of the role of the aqueous veins in the etiology and pathogenesis of glaucoma (see ref. 5, pp. to show the backflow of blood into the canal, as observed gonioscopically by Bangerter and Goldmann.[17] In some cases, changes in these outlets may even be the primary cause for the increase in intraocular pressure (figs. 7, 8).

In order to discuss the role of aqueous veins in the etiology of glaucoma, we may use Sugar's[14] classification of glaucoma. Between the groups "failure of osmotic forces" and "mechanical closure of the chamber angle," it may be justifiable to insert: "occlusion of aqueous veins by different pathologic conditions in the limbal region." These conditions include keratitis, scleritis, tumor growth, and a possible idiopathic narrowing of the outlets of Schlemm's canal. Cases of appar-

ently primary glaucoma caused by this narrowing of the outlets should be classified as secondary glaucoma.[5] (Table 3.)

In the group designated glaucoma secondary to cataract surgery, a blocking of aqueous veins by scar formation adjacent to the cataract incision is to be considered a possible cause of secondary glaucoma. In such a case, the increase of intraocular pressure may not, or at least not solely, be due to mechanical closure of the chamber angle. Along the corneoscleral limbus, numerous outlets of Schlemm's canal seem to be available for intraocular-fluid elimination; even if all outlets situated along the incision should become obliterated by scar formation, those situated in the unsevered part of the limbus still could continue to eliminate aqueous humor. In border-line cases, however, where intraocular pressure is near the upper limit, severing of a part of the outlets during surgery may suffice to produce a postoperative increase of intraocular pressure.

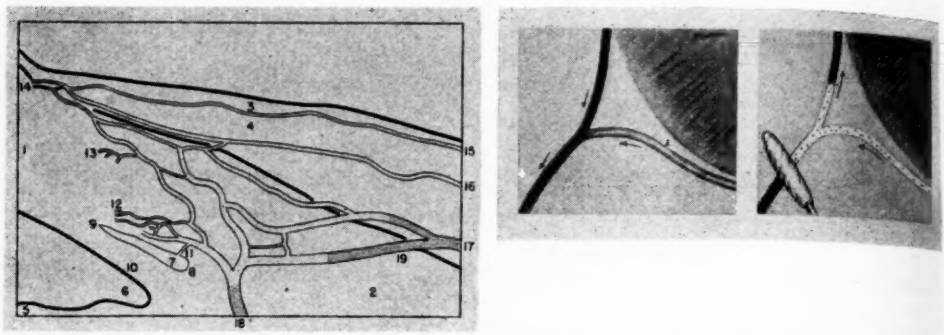

Fig. 5 (Ascher). POSITIVE GLASS-ROD PHENOMENON. *Diagram:* After compression of the recipient vessel, clear fluid enters the blocked section and, in a reversal of current direction, expels the blood corpuscles from the recipient vessel (note arrows in drawing). Expulsion of red cells is the essence of the positive glass-rod phenomenon. *Drawing:* A large, pale vessel runs along the nasal lower limbus and eventually joins a regular conjunctival vein. Immediately after compression, practically all red blood cells leave the pale vessel and the adjacent section of the recipient vein. Both become as clear as water. The red blood cells retreat in an upward direction (note arrows).

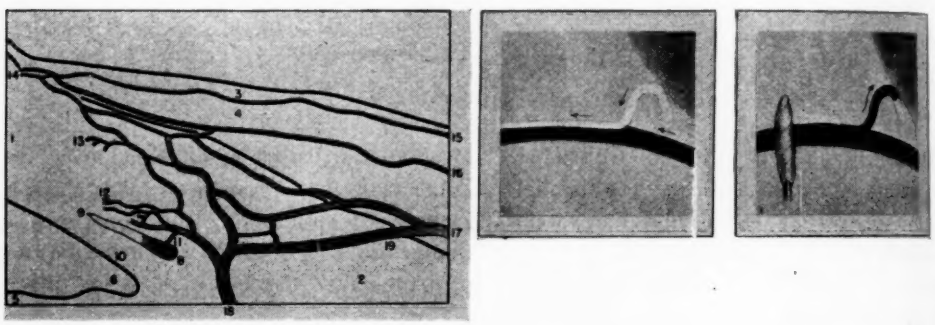

Fig. 6 (Ascher). NEGATIVE GLASS-ROD PHENOMENON. *Diagram:* After compression of the recipient vessel, red blood cells enter the aqueous vein in a direction opposite to that of the previous aqueous flow. Blood may enter the canal of Schlemm (7). *Drawing 1:* At the 7-o'clock position, near the limbus, an aqueous vein joins its recipient vessel to form stratified current. *Drawing 2:* After compression of the recipient vessel, the stratification disappeared and the red blood cells entered the aqueous vein in a direction opposite to that of the previous aqueous flow (note arrows). Entrance of red blood cells into the canal of Schlemm is probable.

Up to the present time investigators have not ascertained whether or not all of the 20 to 30 outlets of Schlemm's canal are equal in physiologic value. Anatomic differences, as demonstrated by Theobald, are rather definite,[18] with diameters of the single outlets varying between 5 and 50 mikrons, that is, in a ratio of 1 to 10. It seems reasonable to assume that an outlet measuring 50 mu in diameter will be more important for the intraocular-fluid elimination than another outlet only one tenth as large. Presence or absence of visible fluid elimination in human eyes may well be due to differences in the size of the outlets in different individuals. The location of the visible fluid elimination, that is the site of an individual aqueous vein, most probably also depends mainly upon the size of the single outlet from the canal of Schlemm. It is possible that, in some eyes, a great number of outlets are constantly eliminating aqueous humor; whereas, in other eyes, only a few outlets or even only one outlet may carry the main bulk of it (ref. 7, p. 1192).

In eyes of the latter type, surgical or traumatic severing of one of these main channels may initiate a disastrous increase of intraocular pressure. Gartner[9] seems to have been the first surgeon who paid attention to the possible danger connected with damaging an aqueous vein during an eye operation.

Engorgement of the venous drainage as a possible cause of glaucoma has been discussed in a previous publication (see ref. 16, p. 1310). The possible influence of local, as well as systemic, increase of venous blood pressure on intraocular pressure was discussed, and the role of

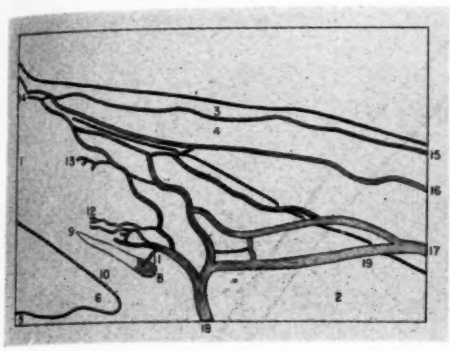

FIG. 7

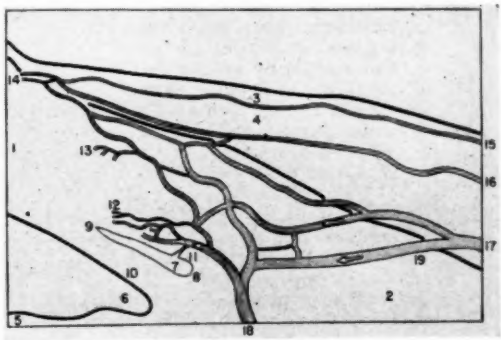

FIG. 8

Fig. 7 (Ascher). BLOOD MAY ENTER SCHLEMM'S CANAL in the presence of any of the following conditions: Inflammation (Salzmann, Trantas, Troncoso); rubeosis iridis (O. Kurz); strangulation (Schlemm); pressure of the gonioscopic lens (Sugar, Bangerter and Goldmann); decrease of intraocular pressure (Kronfeld and associates). Although Schlemm's canal has been thought to contain either colorless fluid or blood, considerable evidence has accumulated that it may contain separated layers of each of them.

Fig. 8 (Ascher). GLAUCOMA AND BACKFLOW OF BLOOD INTO THE CANAL OF SCHLEMM. In eyes with normal intraocular pressure, blood easily enters the canal of Schlemm and most probably does so during the negative glass-rod phenomenon. In eyes with primary compensated glaucoma, aqueous veins fail to show the positive glass-rod phenomenon. Gonioscopically, entrance of blood into the canal should be expected. Bangerter and Goldmann, however, stated that in glaucomatous eyes blood rarely entered the canal. They found: In 50 eyes with normal intraocular pressure, 20 eyes showed backflow into the canal, whereas in 40 glaucomatous eyes, only 2 eyes showed the backflow. Backflow into the canal is more common in eyes with normal pressure. Narrowing of the outlets (11) may cause the absence of backflow into the canal and the absence of the positive glass-rod phenomenon in eyes suffering from primary compensated glaucoma.

the aqueous veins in pulsating exophthalmos and in facial hemangioma was mentioned along with the importance of aqueous veins for the fluid elimination in hydrophthalmic eyes.

Sugar stressed the fallacy of considering vascular congestion or lack of it as a criterion in the classification of glaucoma (see ref. 14, p. 329) and quoted Barkan as having the same opinion. This standpoint seems to be confirmed by the consideration that early signs of congestion may be found in practically every case of compensated glaucoma under biomicroscopic examination of the aqueous veins (see ref. 5, pp. 1076-1077). This certainly does not mean that the clinically so important distinction between compensated and congestive glaucoma should be disregarded. Its value for therapeutic decisions and for the choice of the operation cannot be overestimated. Fundamentally, how-

TABLE 3

CLASSIFICATION OF SECONDARY GLAUCOMA
Modified from Sugar's table (1942)

A. Failure of Osmotic Forces
  1. Arteriosclerosis in afferent vessels of the canal of Schlemm
  2. Obstruction of trabecular spaces
    a. Glaucoma capsulare of Vogt
    b. Pigment accumulation
    c. Obstruction by cellular debris
    d. Blocking by tumor growth
  3. Increased protein content of the aqueous humor (uveitis, trauma)
  4. Vascular changes and toxic effects of:
    a. Vitreous hemorrhage
    b. Occlusion of central retinal vein
    c. Diabetic rubeosis of iris
B. *Occlusion of Aqueous Veins (Canal Outlets)*
  1. Keratitis
  2. Scleritis
  3. Tumor growth
  4. Narrowing or obliteration of outlets
C. Mechanical Closure of the Chamber Angle
  1. Shallow-angle glaucoma in:
    a. Acute glaucoma
    b. Glaucoma due to lens intumescence
  2. Glaucoma following cataract surgery from:
    a. Blocking of the chamber angle
    b. Obliteration of *severed aqueous veins* (canal outlets) (See B. 4)
D. Dislocation of the Lens
E. Lack of Communication between Posterior and Anterior Chambers
  1. Seclusio pupillae
  2. Total posterior synechia
F. Obstruction of Venous Drainage
  1. In the vortex veins
  2. *In the aqueous veins (canal outlets)*:
    a. Increased systemic venous pressure (Colomba)
    b. Naevus flammeus of face
    c. Pulsating exophthalmos
G. Local Hyperemia
  1. Traumatic glaucoma
  2. Reflex hypertonia (Magitot, Brault)
  3. Histaminelike reaction in epidemic dropsy
H. Congenital Anomalies
  1. Hydrophthalmos (malformation of the canal or/and of *its outlets?*)
  2. Juvenile glaucoma
  3. Neurofibromatosis

In this table, *italics* indicate the role of the aqueous veins. For explanation, see also previous publications. [5,16]

ever, it must be stated that, on biomicroscopic examination, early signs of vascular congestion are found in eyes suffering from an otherwise unquestionably compensated glaucoma (table 3).

Aqueous veins as pathways of decompensation

Leber, Maggiore, and Theobald (see ref. 7) described collaterals, connecting both venous districts, which finally empty into the vortex veins and into the anterior ciliary veins, respectively. While the majority of the veins of the human ciliary body are drained into vessels which finally empty into the vortex veins, a part of the veins that leave the ciliary muscle pierce the sclera and empty into the anterior ciliary veins. Although seen and described by Leber, these connections are not clearly visible in his well-known scheme which has been reproduced in almost every textbook of ophthalmology. They are better visible in Maggiore's and Theobald's illustrations, as well as in Duke-Elder's reproduction[19] of Maggiore's drawing, and in the reproduction of the same drawing published by Rollin[20] in the French "Traité d'Ophthalmologie." These connections between two otherwise independent venous regions have rarely been mentioned in the glaucoma literature. They are, however, highly significant for the understanding of the mechanism of decompensated (or congestive) glaucoma (fig. 9).

With an increase in intraocular pressure, increasing quantities of blood that should leave the choroid by way of the vortex veins are forced into a collateral detour via the scleral plexus into the anterior ciliary veins. Thus, the venous return takes place partly through channels which normally do not take care of blood deriving from the choroid. Years ago, Heerfordt[21] discussed the possibility that increased intraocular pressure may lead to compression of the intrascleral part of the vortex veins, an assumption which emphasized the importance of vortex veins and of their connections leading to the anterior ciliary veins for an understanding of the mechanism of congestive glaucoma.[22] He assumed that increase of intraocular pressure may exert a valve-like effect on the origins of the vortex veins, forcing blood that normally should leave the vortex vein backward and into the anterior ciliary veins. Although Heerfordt's theory was not given much consent

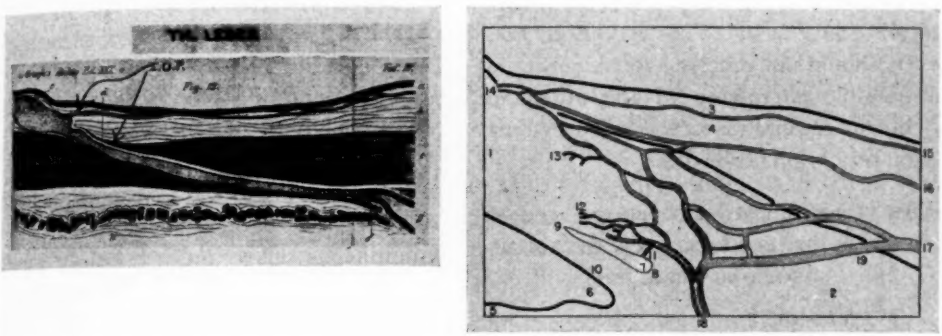

Fig. 9 (Ascher). AQUEOUS VEINS AS PATHWAYS OF DECOMPENSATION. *Drawing:* With increase of the intraocular pressure, the vortex veins become compressed (note arrow). *Diagram:* With compression of the vortex veins, blood is forced into the scleral meshwork (12, 13). Here it assumes a direction opposite to that of the aqueous outflow (arrows).

(mainly because his hypothesis regarding the alleged valve-like effect on the vortex-vein origin was not confirmed), the significance of the collaterals connecting both venous regions (the one draining into the vortex veins and the other, emptying into the anterior ciliary veins) cannot be questioned.

It may well be that the nonappearance of the positive glass-rod phenomenon[5, 16] in glaucomatous eyes can be considered, at least in some of the cases, an early sign of congestion in the collateral pathways which connect the drainage system of the vortex veins with that of the anterior ciliary veins. This reflection, however, should not preclude consideration of a possible narrowing of the outlets of Schlemm's canal, as described previously (see ref. 5, pp. 1083-1087).

The clear fluid observed in aqueous veins is not produced by a skimming of red blood cells

One question remains to be answered. It might be doubted that the clear fluid seen in aqueous veins really is aqueous humor, sometimes clear, sometimes mixed with varying amounts of blood. Another interpretation might have been proposed; namely, that in the narrow vascular passages surrounding the corneoscleral junction of the human eye, a mere skimming off of plasma from red blood cells may occasionally take place. In this case, the clear fluid observed in aqueous veins would be blood, deprived of all, or of a part of, its red cells. In other words, it would be plasma without, or with a subnormal content, of red cells. I have rejected this hypothesis (see ref. 7, p. 1185) because of the anatomically recognized connections between the canal of Schlemm, the intrascleral vascular meshwork, and the episcleral and conjunctival veins. The phenomena observed after compression of the recipient vessels also favor the assumption that aqueous humor is present in the aqueous veins. Vail proposed to reach a final decision by using fluorescein as a tracer. Before I could start on experiments of this kind, Goldmann[10] succeeded in demonstrating that the limpid fluid streaming in the aqueous veins was not plasma but aqueous humor. He performed experiments on persons whose aqueous veins were very distinct. Five c.c. of a 10-percent solution of uranin, which is identical with fluorescein, were injected intravenously. Goldmann made his observations of the aqueous veins by means of a slitlamp microscope with its rheostat maximally opened and with intercalation of a Corning ultraviolet filter. Whereas vessels containing blood soon showed a yellowish-green hue, the aqueous veins remained clear and colorless. In recipient vessels, Goldmann was able to distinguish two or more parallel strata, a greenish, sanguineous phase and a colorless, aqueous one. Using a 20-diameter magnification, he saw a uniform greenish color only after a complete mixing of the aqueous and sanguineous phases, which took place a few millimeters beyond the junction of the aqueous vein and its recipient vessel.

Goldmann's observations, performed after intravenous uranin injection, proved that the aqueous veins contain intraocular fluid and not plasma, partly or completely deprived of red blood cells. After intravenous administration, uranin circulates with the blood, confined to the plasma. It would appear even in skimmed up plasma. Therefore, the lack of color in aqueous veins after intravenous administration of uranin leads to the conclusion that these vessels do not contain blood deprived of red blood cells but intraocular fluid with varying amounts of blood.

The response of animal and human eyes to oral and to parenteral fluorescein administration has been studied by several investigators. The most exact figures

seem to be those reported by Lindner[23] who, after oral administration of 4 gm. of uranin, observed normal human eyes with the aid of the corneal microscope. The interval between administration of the dye and its appearance in the anterior chamber was 15 to 30 minutes; the highest intensity of the green hue, however, was found 1½ to 2 hours after intake of the dye. This maximum lasted for one to two hours, and the complete resorption of the green color from the anterior chamber did not take place before one, or even two, days had elapsed. Using colorimeter tests, Lindner stated that the uranin concentration in the aqueous humor reached 1:8,000,000 to 1:3,000,000. In the initial stages of the experiments, the concentration of uranin was markedly higher in the blood as compared to that in the aqueous humor; later on, however, the uranin level of the aqueous humor surpassed that of the blood.

These observations would indicate that it is imperative to perform experiments, similar to Goldmann's, soon after the administration of uranin, especially if the dye is introduced intravenously; for by this method the interval between the administration of the dye and its entrance into the anterior chamber is shorter as compared to the interval observed after oral intake. In albinotic eyes, the green color appears in the anterior chamber while the uranin injection is being performed.[13] The fact must be considered that uranin will pass through the blood-aqueous barrier twice: first, from the capillaries into the aqueous humor; then, from the aqueous humor into Schlemm's canal and possibly into intraocular capillaries which finally will return the dye into the venous circulation. If the wait is too long, it may be possible to see green color in the aqueous veins and none in the regular veins, indicating the resorption of the dye via the canal of Schlemm and the intrascleral meshwork. Up to the present time, this phenomenon has not been described.

Goldmann[10] performed another important experiment to show that the contents of the aqueous veins are really aqueous humor and the aqueous veins are accessible from the anterior chamber of the human eye. In repetition of the famous animal experiments performed by Seidel (see ref. 7), Goldmann injected India ink into the anterior chamber of an eye that was to be enucleated because of a uveal sarcoma. Previous to the injection of the ink, an aqueous vein was located in the nasal episcleral region of that eye. After the instillation of a cocaine solution and the aspiration of a small amount of the aqueous humor contained in the chamber of the sarcomatous eye, an ana-partes mixture of saline solution and Guenther-Wagner Pertusche (a brand of India ink) was injected into the anterior chamber. The intraocular pressure was reduced after the injection of the ink and, although the regular episcleral vessels maintained their normal red color, the previously located aqueous vein showed a black tint.

Thus, for the first time, it was demonstrated that an aqueous vein could be filled with a material introduced into the anterior chamber. The most striking objection to Seidel's experiments using anterior-chamber injections was raised by Weiss who (see ref. 7) stated that this method could destroy natural barriers separating the anterior chamber from the canal of Schlemm or from intrascleral veins, either during the preliminary aspiration of aqueous humor or during the injection of the dye. It is difficult to understand why this possible destruction should have occurred, in Goldmann's experiment, just on the site of the previously located aqueous vein which turned black while the regular episcleral veins

maintained their normal red color.

Both types of experiments (uranin administration and ink injection) prove that the aqueous veins are accessible from the anterior chamber, as well as that these veins really contain aqueous humor. They do not prove, however, that there is a free communication between the anterior chamber of the human eye and the canal of Schlemm.

Visibility of aqueous veins without the use of the corneal microscope

In most instances, the aqueous veins proper are too small to be recognized without the aid of the slitlamp microscope. Some of them, however,—namely, those that carry a stratified current and attain a diameter exceeding that of the smallest precapillaries—can be seen with a 10-diameter magnifying loupe under good focal illumination. Their size and the presence in the same vessel of a sanguineous and a clear phase make them readily recognizable with the aid of the loupe.

During the autumn of 1945 and the spring of 1946, 400 unselected patients with quiet eyes were examined for the presence of aqueous veins detectable without the corneal microscope. Of these patients (most of whom came in for a test of refraction) 57 showed aqueous veins when examined with the simple magnifying loupe. Thus, with the loupe 14.25 percent of all uncongested eyes were found to show aqueous veins; whereas, 26.78 percent showed them when observed under the slitlamp microscope.[7]

It should be mentioned that, with this method of examination, a recipient vessel might sometimes have been counted instead of an aqueous vein proper. The presence of a recipient vessel, however, always is indicative of the presence of an aqueous vein. It is, therefore, valid to assume as correct an estimate of 14.25 percent for eyes showing aqueous veins (or at least recipient vessels) under loupe observation.

Seasonal differences in the occurrence of aqueous veins

Although observation of the individual eye revealed the presence of one or of a few vessels charged with a continuous or intermittent elimination of aqueous humor (see ref. 1, p. 35; ref. 7, p. 1179), and although the same aqueous vein could be recognized after intervals ranging from a few months to 2½ years (see ref. 5, p. 1077),* the occurrence of the aqueous veins seemed to change with the seasons of the year.

The 400 patients mentioned were seen at different times of the year. Two hundred were examined during the months of November and December of 1945, and 200 during March and April of 1946. As has already been stated, these examinations were performed without the corneal microscope and with only a 10-diameter magnifying loupe under good oblique focal illumination. At this lower magnification, an average of 14.25 percent of easily visible aqueous veins (or at least recipient vessels of an aqueous vein) were observable. In the autumn group, however, the percentage of aqueous veins was only 10.0; whereas, in the spring group, it was as high as 18.5 percent.

The assumption that the occurrence of aqueous veins could vary seasonally does not explain this numerical difference. The histologic substrata of the visible intraocular-fluid elimination (see ref. 7, p. 1179) cannot possibly change with changes of climatic factors. What, however, may change is the degree of difficulty encountered in finding vessels differing in color from the regular conjunctival and subconjunctival veins. The visi-

* Since that time, aqueous veins have been observed up to a period of 4½ years.

bility of the aqueous veins and of their recipient vessels, may well be influenced by at least one of the climatic factors; namely, by seasonal differences in illumination (see ref. 7, p. 1200). An eye exposed to bright light often shows an increase of the clear fluid contained in its aqueous veins and, occasionally, even an increase of the speed with which the clear fluid is flowing in them; however, in many eyes, darkness produces the opposite effect—namely, an increase of the red-blood-cell content of the aqueous vein and, occasionally, a retardation of the flow in the aqueous vein. In this connection, I should mention that, in eyes blind from tabetic optic-nerve atrophy, I have often found an extremely slow movement of the fluid streaming in the aqueous veins. The greater degree of brightness of the sky during the months of March and April might be responsible for the greater ease of finding aqueous veins during these months than during the months of November and December. There may also be a connection between the ease of finding the aqueous veins and the occurrence of conjunctival diseases. The incidence of slight conjunctival irritations may be higher during the fall and early winter than in the spring; therefore, the well-known effect of conjunctival hyperemia on aqueous veins (see ref. 16, p. 1314) will make them appear less conspicuous, or even completly disappear, in those periods of the year when external factors favor the development of any kind of conjunctival hyperemia. This may serve to explain the difficulty encountered by some ophthalmologists in finding aqueous veins at all. In discussing the extremely rare observation of aqueous veins in the eyes of patients admitted to the Utrecht University Eye Clinic, Fischer[13] agreed to my tentative explanation that, after so many months of starvation, the conjunctivas of all people coming to this Clinic were more or less congested. Hyperemia in conjunctival or episcleral vessels tends to conceal the presence of aqueous veins by adding red cells to the clear stream. Therefore, anything that may increase the red-cell content in the aqueous veins will make recognition more difficult. If nutritional or climatic factors favor the incidence of even slight conjunctivitis cases, they may produce the impression of scarcity or even absence of aqueous veins by making the clear fluid indiscernible.

Summary

In 1941, for the first time by means of the biomicroscope, aqueous humor was seen to stream through conjunctival and episcleral veins of the normal human eye. Vessels containing a clear fluid, sometimes mixed with varying amounts of blood, can be found in at least one third of all quiet human eyes with the use of the corneal microscope and slitlamp illumination. With the aid of a 10-diameter magnifying loupe and good oblique illumination, they are detectable in more than 14 percent of all eyes not injected. Emerging from the limbal meshwork, from the depth of the scleral tissue adjacent to the limbus, or from a scleral emissarium, these clear vessels join conjunctival or subconjunctival veins. In the recipient vessel, they produce either a marked dilution of its blood content or a characteristic pattern of stratification with two, three, or more differently colored layers that run parallel to one another along the vessel wall. The colorless vessels were termed aqueous veins. They are biomicroscopically visible pathways connecting Schlemm's canal and the intrascleral meshwork with conjunctival and subconjunctival veins. Not all quiet human eyes show aqueous veins owing to the fact that aqueous humor, upon leaving the canal of Schlemm, may become rapidly and completely mixed with the blood which is

contained in the intrascleral meshwork. If, however, clear fluid can reach the episcleral or conjunctival veins without the previous addition of too many red blood cells, an aqueous vein will become visible. Anatomic differences in the outlets of Schlemm's canal are rather definite, and it seems reasonable to assume that an outlet measuring 50 mu in diameter will be more important for the elimination of intraocular fluid than another outlet having only one tenth of this diameter. It is possible that, in some normal human eyes, a great number of outlets are constantly eliminating aqueous humor; whereas, in other eyes, only a few outlets or even only one, may carry the bulk of fluid. In eyes of the latter type, surgical or traumatic severing of one of these main channels may initiate a disastrous increase of intraocular pressure. The possible role of the aqueous veins in the etiology and classification of glaucoma was discussed. Observations on glaucomatous eyes led to the working hypothesis that a transient or permanent narrowing of the outlets of Schlemm's canal may be connected with the presence, or even may be responsible for the development, of increased intraocular pressure in certain eyes. Clinical observations and reflection suggest the significance of aqueous veins in the mechanism of decompensated glaucoma.

Many ophthalmologists have had difficulty in recognizing the aqueous veins; whereas, others have confirmed their occurrence and significance. Photographs of recipient vessels have corroborated the presence of highly diluted blood in these vessels, as well as the influence of drugs on the elimination of intraocular fluid through the aqueous veins.

Protracted observation of the veins surrounding the corneoscleral junction will always reveal that one or more individual channels are continually charged with the elimination of intraocular fluid. Physiologic factors and climatic differences in part concur in their effect and in part exercise the opposite influence on aqueous veins. Once located, the particular aqueous vein remains discoverable at its original location after months and years, and retains its characteristic qualities. Apparent differences in the incidence of aqueous veins, when searched for with a 10-diameter magnifying loupe at different seasons of the year, are due to differences in the red-cell content and to the greater difficulty of recognizing an aqueous vein when there is conjunctival congestion. In eyes blind from tabetic optic-nerve atrophy, the movement of the fluid streaming in aqueous veins is often slow.

The question as to whether aqueous veins contain aqueous humor or blood deprived of all, or part, of its red cells, has recently been answered by Goldmann. He stated that, after intravenous injection of a 10-percent uranin solution, the aqueous veins remained colorless while the blood running in the recipient vessels, in conjunctival and in subconjunctival veins, showed the greenish-yellow hue of the dye. India ink, injected into the anterior chamber of an eye with a uveal sarcoma, appeared in a previously located aqueous vein only and not in any of the other vessels.

The physiologic and clinical significance of the aqueous veins should be acknowledged. The term aqueous veins should be accepted for the biomicroscopically visible part of the pathways which are charged with intraocular-fluid elimination from the canal of Schlemm via intrascleral meshwork to the conjunctival, subconjunctival, and anterior ciliary veins.

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Discussion

Sir Stewart Duke-Elder, chairman (London, England): I should like to thank Dr. Ascher for his able presentation—not only an exceedingly interesting subject, but very important, and a subject on which there ought to be some study.

I want to ask him one question. You started off by eliminating the arterial system entirely. Do you agree with Dr. Friedenwald that there are direct arterial aberrant vessels in the canal of Schlemm.

Dr. Ascher (closing): I do not dare to answer that question because I do not have any pertinent experience of my own.

From the papers published on this subject, I do believe that it is very possible that these vessels described by Friedenwald are not only present but that they also fulfill the physiologic function as described or ascribed to them by Friedenwald.

EXPERIMENTAL DINITROPHENOL CATARACT*

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Cataract following the ingestion of dinitrophenol in human patients was first reported in 1935.[1, 2] Within the following six years, 177 cases had been reported in the literature.[3] The patients who developed dinitrophenol cataracts were obese, were almost all women, and were in a younger age group than those in whom cataracts were ordinarily seen.[4] These facts suggest that variations in metabolism may be significant in the development of the cataracts.

Thorough experimentation on laboratory animals prior to the release of dinitrophenol for medical use was carried out by Tainter and his fellow workers at Stanford Medical School. Further careful work was done following the reports of dinitrophenol cataracts in humans. In no instance was it possible to produce cataracts in the ordinary laboratory animals (specifically rats, rabbits, guinea pigs, and dogs);[5] nor was it possible to produce experimental cataracts on feeding dinitrophenol to animals deficient in vitamins A, B_2, or C.[6] The incidence of cataracts could not be increased when dinitrophenol was administered in conjunction with such cataract-producing agents as lactose and galactose.[7] These facts again suggested that variations in metabolism accounted for the failure of animals to develop dinitrophenol cataracts. It is significant that in all cases the species used were mammalian.

In 1944, Robbins[8] reported that chickens and ducks on a diet of 0.25-percent dinitrophenol developed marked lens opacities within eight hours. These lens opacities were sufficiently dense to be seen by the naked eye, although they cleared almost entirely within 24 hours after the dinitrophenol diet was started and while the birds were still on the 0.25-percent dinitrophenol diet. This work was quickly confirmed.[9] The lens opacities were limited to the anterior and posterior subcapsular regions. The posterior subcapsular area was more densely opaque than the anterior. The nucleus and the remainder of the lens cortices remained entirely clear. No abnormalities other than in the lens were noted by slitlamp microscopy. The opacities developed in 100 percent of young chicks on the 0.25-percent diet, but with less regularity in older chickens on the same concentration of dinitrophenol.[10] They even developed on concentrations of dinitrophenol as low as 0.05-percent, but with less frequency.

Now, at long last, experimental dinitrophenol cataracts had been produced, but they had been produced in avians, not mammals, and they were transient, not permanent.

Experiments on obese mice

One of the significant facts in human patients who developed dinitrophenol cataracts is that they were all obese. In previous experimental studies, obese animals had never been used. To determine whether or not factors associated with obesity may play a part, a strain of congenitally obese mice was fed dinitrophenol. These adipose mice have been used for studies in obesity for the past 20 years.[11] The mice were all yellow, and

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the gene for adiposity was apparently associated with the yellow color. They were all heterozygotes since the yellow gene is lethal when homozygous. In conjunction with the adiposity, and probably responsible for it, was a definite tendency for the yellow mice to eat more and be less active, as is often the case with adipose humans.[12] In all other respects, the obese yellow mice did not seem to differ from the ordinary nonobese varieties.

In this experiment, 40 fat, yellow mice were put on their usual diet of Tioga meal, but 0.1-percent dinitrophenol was mixed with it. Forty control fat, yellow mice were placed on the diet of Tioga meal without the dinitrophenol. The dosage of 0.1-percent dinitrophenol in the diet was selected because this was previously determined by Tainter[13] as a concentration sufficient to decrease the growth rate and final weight without decreasing the life span of white rats. This concentration, therefore, was believed to be sufficient to affect the metabolism without being lethal to the yellow mice.

The animals used were 8 to 10 months old (younger middle age). They were examined by slitlamp microscopy before the experiment was started and at periodic intervals thereafter; they were weighed weekly. Many mice present fine, suture-line opacities that do not develop into immature or mature cataracts and occur regardless of skin color, weight, or diet. In the light of this fact, these fine, suture-line opacities were ignored.

Three of the 40 mice on the diet with dinitrophenol developed cataracts that were immature within four to eight weeks after the diet was started. These cataracts were first seen as fine posterior subcapsular opacities; then the nucleus became milky in association with the development of definite cortical spokes. No other pathologic changes were observed in the eyes with the development of the cataracts. None of the 40 control animals from the same colony developed cataracts.

Although the incidence of three cataracts out of 40 animals on dinitrophenol (7½-percent) is admittedly small, this is comparable to the incidence of thallium cataract in rats, which is 11 percent.[14] It is also comparable to the incidence of 7.4-percent cataracta raphanica in patients with ergot poisoning.[15] The incidence of 7½-percent of dinitrophenol cataracts in congenitally obese yellow mice is definitely higher than the presumed incidence of dinitrophenol cataract in humans. This has been estimated to be 0.86-percent by Horner.[5]

The time of onset of the cataracts in the obese mice (four to eight weeks after the dinitrophenol was started) was also comparable to the time of onset of thallium cataract in rats (six weeks).[14]

In human subjects, cataract formation often occurred with dramatic suddeness some time after the dinitrophenol was discontinued. In order to determine whether or not a comparable phenomenon would occur in the congenitally obese mice the dinitrophenol was discontinued in 13 of the mice after six months of dinitrophenol diet. In no instance did cataract formation occur during an additional four months' period of observations.

Experiments on other mice

As previous experimental work with dinitrophenol feedings had been performed on mammals other than mice, it was necessary to demonstrate that cataracts did not develop in ordinary mice that were not obese. Twenty albino mice were put on a 0.1-percent dinitrophenol diet and 20 albinos were kept as controls. Twenty black mice were also placed on the 0.1-percent dinitrophenol diet, to rule out possible differences due to pigmenta-

tion. No cataracts developed except for one albino mouse which developed a cataract just before its death after 11 months of dinitrophenol feedings. This is not comparable to the cataracts which developed after only four to eight weeks in the younger mice.

The question logically arises as to why chickens are so much more susceptible to the formation of dinitrophenol cataracts than are the obese mice. Is this difference due to higher dosages of the drug used in some of the chickens? Is it due to the difference in age of the chicks and the mice, or is it due to differences in the temperatures of the two species? In an attempt to answer these questions, the following experiments were performed.

Although a 0.25-percent dinitrophenol diet is lethal to mice within a short time, experiments were undertaken to determine whether this dosage would produce cataract formation in mice within less than 24 hours as had occurred in chickens.

Six ordinary albino mice were put on a 0.25-percent dinitrophenol diet. They were examined before the diet was started and eight hours later. No cataract formation was present in any of the mice at this time. All six died shortly thereafter, as the dosage of 0.25-percent dinitrophenol was lethal. Six congenitally obese yellow mice were put on the same diet and examined at the same intervals. Their eyes also remained clear, and they likewise died shortly after the eight-hour period. We may conclude that 0.25-percent dinitrophenol does not cause rapidly developing cataracts in either obese or ordinary adult mice, although it did cause this type of cataracts in chicks.

In view of the fact that young chicks were more prone to develop cataracts than adult chickens, five-to six-week-old mice were also put on 0.25-percent dinitrophenol. All eight of the mice were free of cataracts nine hours after the diet was started. The 0.25-percent dinitrophenol diet was continued for one week, and repeated observations were made during this time. At the end of this period, two of the mice had died, but all were free from cataract formation. The age of the mice, then, did not seem to be a factor in the development of the type of cataract observed in chickens on a dinitrophenol diet.

Effects of temperature

The normally higher avian body temperature suggested that this may have been a factor in the predisposition of the chicks to cataract formation while on a dinitrophenol diet. It had already been shown that the toxicity of 2:4 dinitrophenol on mice is increased by raising the environmental temperature to 40°C. and lowered by decreasing the environmental temperature to 6°C.[16] Accordingly, 10 congenitally obese yellow mice were placed in an incubator with the environmental temperature kept at 38 to 38.8°C. Five of the group of 10 mice were also put on a diet of 0.25-percent dinitrophenol, while the other five were kept in in the incubator on a normal diet as controls. The body temperatures of the incubated mice on DNP were variable but tended to be higher than the readings noted in other group. After eight hours of incubation of both groups, neither the one on dinitrophenol nor the one without it developed cataracts upon examination by slitlamp microscopy. All of the mice subjected to both incubation and dinitrophenol died shortly thereafter and, consequently, the experiment could not be continued. Differences in temperature, then, did not seem to be the factor which accounts for the difference in the susceptibility of mice and chicks to transient cataracts.

One cannot draw definite conclusions from an experiment in which only 3

of 40 obese mice developed cataracts in two months or less. Nevertheless, the absence of cataract formation in thin mice (except one moribund mouse which had been on therapy for almost a year) suggests that obesity may be a definite factor in cataract formation associated with dinitrophenol therapy. It was necessary to work with relatively small numbers of mice because of the need of numerous time-consuming slitlamp examinations.

As previous studies had demonstrated that chicks on a diet of 0.25-percent dinitrophenol developed a transient cataract within eight hours, the question naturally arises as to why the chickens are markedly susceptible to a transient dinitrophenol cataract, whereas obese mice are slightly susceptible to a permanent dinitrophenol cataract,. and other mammals are not at all susceptible. It was not the dosage, since chicks develop cataracts on concentrations as low as 0.05-percent, although with less regularity, and mice do not develop the cataracts on concentrations as high as 0.25-percent. It is not the age factor, because old chickens do develop dinitrophenol cataracts, whereas young mice on comparable doses do not develop them. It probably is not the higher body temperature of avians, for mice placed in an environmental temperature of 38° to 39°C. did not show cataracts while on the 0.25-percent dinitrophenol diet.

It may be that the transient opacity in the chick is due to a relative anoxia produced by the dinitrophenol, since dinitrophenol increases the oxygen consumption. Cataracts have been produced in a decompression chamber in rats and rabbits.[14a] It may be that this effect is due to an increase in the lactic acid, which was also demonstrated under these circumstances. One may speculate that this produces a colloidal change which has not gone far enough to be irreversible.

Direct injection experiments

We now may ask the question: Is the transient cataract produced in chicks by dinitrophenol a direct effect of the drug on the lens, or it is due to some product, toxic to metabolism, resulting from the ingestion of dinitrophenol? Is there a difference in susceptibility of the avian lens and the mammalian lens to dinitrophenol cataract, or is this apparent difference due to factors elsewhere than in the lens?

To answer these questions, sodium 2:4 dinitrophenol was injected into the anterior chambers of young chickens. Dense anterior subcapsular cataracts were found 20 to 40 minutes after the direct injection of the dinitrophenol. The solutions of dinitrophenol had been rendered isotonic and buffered to pH7.3, and were used in dilutions of 1:1,000, 1:5,000, and 1:50,000. A control solution of the agents used to attain isotonicity and the buffered state was injected into the opposite eye of each chick and in no instance did a cataract occur. The average quantity used was 0.04 c.c., and the injection was preceded by withdrawal of the same amount of aqueous. The cataracts were exceedingly dense when unbuffered 1:1,000 dinitrophenol was used; somewhat less dense when buffered 1:1,000 dinitrophenol was used; and even less dense, but very definite, when the buffered 1.5,000 solution was used. The 1:50,000 solution did not cause cataracts when injected in the usual quantity of 0.03 to 0.05 c.c.

Twenty-four hours after the injection these lens opacities had cleared almost completely. Seventy-two hours after the injection, the lenses were entirely clear.

Experimental procedure

Four- to eight-weeks-old, white-leghorn female chicks were used. The eyes were examined

by slitlamp microscopy preceding the injection and were found to be clear in all instances. The chicks were anesthetized with ether, and 0.5-percent tetracaine drops were instilled locally. After puncture through the cornea with a 30-gauge needle and a tuberculin Luer without injuring the iris or lens, 0.03 to 0.05 c.c. of aqueous was withdrawn. Through the same corneal-puncture wound, 0.03 to 0.05 c.c. of the sterile solutions described above was injected. The chickens were examined by slitlamp microscopy at intervals of 15 minutes after the injection for the first two hours, and again in 24 hours and 72 hours.

Within the first 15 minutes, no lens changes were found, but the secondary aqueous was cloudy in both the eyes injected with the dinitrophenol and those injected with the buffer solution used as a control. Approximately 30 minutes after the injection, the dinitrophenol-instilled eyes revealed definite anterior subcapsular opacities. These increased in the succeeding 15 to 30 minutes and then remained unchanged. In some instances a fine posterior subcapsular opacity appeared to be present, but the remainder of the lens was always clear. Twenty-four hours after the injection, the lenses were almost entirely clear except for a very fine anterior subcapsular opacity in some instances. Seventy-two hours after the injection all lenses were entirely clear. In no instance did the control eye exhibit any lens changes.

The buffer-control solution and buffered-dinitrophenol solutions were prepared by the Barnes-Hind Laboratories of San Francisco, as follows:

1. A phosphate buffer solution of pH 7.3 was made according to the following formula:

Sodium acid phosphate	($NaH_2PO_4 \cdot H_2O$)	1.747 gm.
Disodium phosphate	(Na_2HPO_4)	7.653 gm.
Sodium chloride		3.90 gm.
Distilled water q.s.		1,000 c.c.
pH adjustment 7.3 plus or minus 0.02 pH unit		(24°C.)
Freezing point depression —0.569°C.		

2. Sodium dinitrophenol solutions: The following concentrations of sodium dinitrophenol were prepared in the above buffer:
   a. 1:1,000
   b. 1:5,000
   c. 1:50,000
   d. 1:200,000

   Preparation: A 1-c.c. ampul was filled with these four concentrations and also a 1-c.c. ampul containing the phosphate buffer alone as controls. The sealed ampuls were autoclaved at 120°C. for 20 minutes for sterilization. Ampuls from each concentration were checked for sterility on thioglycolate media. All cultures were negative.

It is of interest to compare the concentration of dinitrophenol, which caused a definite cataract when injected into the anterior chamber, with the concentration probably attained after ingestion of sufficient dinitorphenol to cause a definite cataract in the chick. Direct injection of 0.04 c.c. of 1:5,000 dinitrophenol solution consistently produced a cataract. The ingestion of 110 gm. of 0.25-percent dinitrophenol by a 440-gm. chick likewise consistently produced a cataract. If all the dinitrophenol were absorbed, and if it were equally distributed throughout the body, a concentration of 1:1,600 would result. As complete absorption and equal distribution are extremely unlikely, it is probable that the concentration produced by direct injection and by ingestion are similar.

In the light of the fact that dinitrophenol produces cataract by direct injection, and that the concentration which causes cataracts by this method (1:5,000) is comparable with the concentration resulting from ingestion (1:1,600), it is suggested that the effect of dinitrophenol upon the chicken lens is a direct action not dependent upon any intermediate product of metabolism.

It next remained to be determined whether the failure to obtain cataracts from dinitrophenol in most mammals was due to a difference in the reaction of the lens itself to the dinitrophenol or to a difference in the metabolism of dinitrophenol in the mammal as compared with the avian species. The direct injection of dinitrophenol solutions into the eyes of rabbits was, therefore, performed. The injections were done in precisely the same manner as described in connection with the chicks, except that a larger quantity (+0.10 c.c.) was injected, because the anterior chambers were larger. The same type of anterior subcapsular cataract occurred in the same length of time and cleared completely as was the case with the chicks, although the opacity

was not quite so marked in the rabbits as in the chicks.

Rabbits, as well as other mammals, had previously been subjected to feeding experiments with dinitrophenol and, in all cases, no cataracts developed. In order to confirm the absence of cataract formation in rabbits, when fed the same concentration of dinitrophenol as chicks, rabbits were placed on a diet of 0.25-percent dinitrophenol. Although this concentration produced a cataract within eight hours in the avian, it failed to produce any lens changes in the rabbit in eight hours, or at any period thereafter until the observations were discontinued after four weeks

It is suggested that the failure to obtain cataracts in most mammals is due to a difference in metabolism as compared with the metabolism of avians, and not to a difference in the lenses themselves.

Experiments on lens

The next obvious question is whether the action of dinitrophenol is an interference with the metabolism of the living lens or whether it also affects lens tissue *in vitro*. Lenses were removed from chickens, fat mice, and rabbits immediately after the animals had been killed. Removal was effected without injuring the lens capsule and the lenses were immediately immersed in solutions of buffered isotonic (1:1,000) dinitrophenol, unbuffered nonisotonic (1:1,000) dinitrophenol, and a control solution of the buffer material. In no instance could lens opacities be observed within two hours in the lenses from any of these species in any of these solutions. The examinations were performed by slitlamp microscopy in the same manner as in the living eyes as well as by other methods of magnification.

We must assume from the foregoing, that dinitrophenol acts only on the living lens and does not produce cataract *in vitro* with comparable concentrations and in a comparable time.

Summary

Dinitrophenol is estimated by Horner to be associated with the development of cataracts in obese humans in an incidence of 0.86-percent. It is associated with the development of cataracts in obese mice in an incidence of 7.5-percent. The cataract has often occurred in humans after the withdrawal of dinitrophenol therapy; it does not occur in obese mice after the withdrawal of dinitrophenol. It did not occur in ordinary nonobese mice under any circumstances.

Dinitrophenol causes lens opacities in fowl within eight hours after a diet containing dinitrophenol is started. The opacities clear spontaneously while the fowl are still on the diet. In comparable dosages, dinitrophenol failed to cause lens opacities in young or adult obese mice whether or not they were placed in higher temperatures.

The direct injection of dinitrophenol into the anterior chamber of chickens and rabbits causes lens opacities in each within approximately one-half hour. The opacities clear within 24 hours. Rabbits do not develop lens opacities when fed dinitrophenol.

The direct immersion of the lenses of chickens, obese mice, and rabbits in a solution of dinitrophenol does not cause an opacity in a comparable length of time.

Conclusions

The results of these experiments lead to the following conclusions and conjectures:

1. Dinitrophenol acts only on the lens *in vivo* of mammalian as well as avian species.

2. Lenses *in vitro* did not develop this opacity. This may be because: (a) dinitrophenol, when in the anterior chamber, forms another compound which then acts on the lens, or (b) the permeability of the lens capsule is different when the lens is *in vitro* as compared to its normal state, or (c) dinitrophenol interferes with some phase of metabolism of the living lens, such as causing an increased need for oxygen or producing more lactic acid.

3. The failure of mammals to develop the transient opacities observed in fowl is due to a difference in metabolism of the species; it is not due to a difference in the lenses themselves.

4. The variations due to metabolism are confirmed by the occasional occurrence of permanent cataracts in congenitally obese mice. Such opacities did not occur in nonobese mice. This frequency of cataract formation is comparable to the incidence of cataract in obese humans and may explain the previous failures of numerous investigations to produce cataracts in experimental mammals.

5. The difference in incidence of cataracts in fowl and mammals is apparently not due to the difference in body temperature. The age of the animal is little, if at all, related.

Numerous questions related to dinitrophenol cataract remain unanswered. Is the cataract-producing action of dinitrophenol due to its effect on oxidation or on sugar metabolism or to something else? Why does the cataract which develops so rapidly in a chick clear spontaneously while the chick is still on the same concentration of dinitrophenol? Why did cataracts occur with great rapidity in human subjects months after the ingestion of dinitrophenol had been discontinued?

Work is being continued in an attempt to answer some of these vexing problems.

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Discussion

Dr. Clyde A. Clapp (Baltimore, Maryland): As a member of the Commission, I should like to ask how many of the males developed dinitrophenol cataract. Are there any in the literature?

The second question is: What was the difference with the slitlamp in the so-called reversible opacities in the avians, and the permanent opacities that occurred in the mice?

Dr. Bettman: There have been reports of dinitrophenol cataracts in human males in one or two instances. I have forgotten the precise number in the literature. It was not common, but it has been reported.

The slitlamp picture of the reversible cataracts in the chickens was a dense opacity entirely limited to the subcapsular layers of the lens. The remainder of the lens was not at any stage involved.

In the permanent opacities of the mice, the first observable change was the same type of subcapsular opacity, posterior at first, and then anterior; in association with the development of the anterior opacity, or at about that stage, the nucleus begins to get a bit milky and then an opacity develops in the entire lens.

Dr. Conrad Berens (New York, New York): I should like to ask one question. Are the terms "dinitrophenol" and "dinitrocresol" synonymous? A clinician in New York claimed a difference, but two obese women patients who were treated with dinitrocresol developed cataracts rapidly. One was 28 years old, and the other was 60 years old.

Dr. Bettman (closing): The term "dinitrophenol" and the term "dinitrocresol" are not synonymous, but the drugs act, so far as we know, in precisely the same manner. Clinically, dinitrophenol has largely been used in the United States and dinitrocresol has been used largely in Europe. They both produce cataracts, and, as far as I know, they both act in the same manner. The group is usually called "dinitro bodies," because they are so similar in their action.

CATARACTA GLAUCOMATOSA ACUTA*

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Since Vogt[1] first described the entity which he named "Cataracta disseminata subcapsularis glaukomatosa" or "Glaukomflecken" in 1930, only five reports of the condition have been made. No cases have been described in the English or American literature. For this reason, and because of the ease with which their presence may confuse the diagnosis of acute glaucoma during a congestive attack, six cases are herein reported.

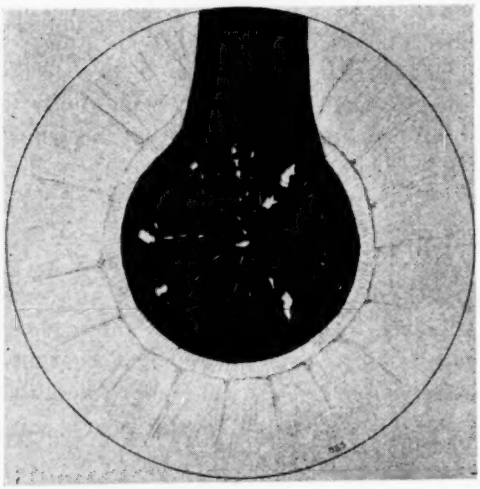

Fig. 1 (Sugar). Diagrammatic drawing of cataracta glaucomatosa acuta (case 5).

This form of cataract consists of multiple, circumscript, white spots of characteristic irregular form and radial arrangement lying beneath the anterior lens capsule. Their color varies from the bluish translucency of very thin lens opacities to a more porcelainlike whiteness. If seen during an acute glaucomatous attack, the lesions are very white. When the intraocular pressure has been reduced, their color is much less intense, and their transparency is increased. The spots have been seen in only the anterior subcapsular cortex, never posteriorly. They do not extend beyond the pupillary zone. None has ever been described as occurring in the region of iridectomies. The axial area is always involved. Here the spots are rounded or dumbbell-shaped and often larger than elsewhere. More peripherally, they are elongated to follow the suture lines of the lens. At the pupil border where the lesions end, the spots are again often large (fig. 1). In general, they vary in size from 0.3 mm. to less than 0.02 mm. (Vogt).

These lens opacities do not change in size with the passage of time. However, since they decrease in intensity immediately after the acute episode with which they are associated, it is conceivable that the very faintest spots may disappear. Once the acute episode is entirely over, the spots do not change in size or color. They do not interfere with the shagreen of the lens. During and immediately after the acute episode, the lesions lie just underneath the capsular epithelium. Later, with the formation of new lens fibers, the spots are pushed deeper into the cortex. Vogt observed in one case that, after five years (from the age of 53 to 58 years), the opacities were 0.5 mm. within the lens cortex. In two cases seen by me at about the time of the acute episode and again after eight years and six years, respectively, the spots occupied a level within the lens cortex equivalent to two thirds of the thickness of the cornea.

There is no significant visual impair-

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ment due to the presence of these thin lens opacities.

The occurrence of lens opacities which Vogt described in his original report was associated only with acute glaucoma. However, since that time, he[2] observed similar opacities in a patient after a severe contusion of the bulb. Similar cases have since been observed by Bücklers (1934),[3] Van Lint (1937),[4] and Sommer (1940.[5] In each of these cases, however, there was evidently a momentary severe ocular hypertension, so that the term "Cataracta glaucomatosa acuta" may still be applied to them. Actually, both types are forms of traumatic cataract. The use of the designation "glaucomatosa acuta" is important to distinguish the entity herein described from other forms of cataract in glaucomatous individuals. Seidenari[6] has included both types in the term "Cataracta glaucomatosa."

The relation between the lens opacities and the acute episode is evident from the fact that the lesions lie directly subcapsularly immediately after the episode. In a case of Kovarskaya and Krolh,[7] the lens was found to be entirely normal when seen two days before an attack of acute glaucoma, following which the opacities were found. Vogt found 14 instances of these opacities among 74 patients with acute glaucoma which were seen by him between 1930 and 1937.

Vogt believed the lens opacities to be due to exudation. My own view is that the lesions are due to traumatic dissolution of the most delicate terminal portion of the lens fibers at the suture areas, in the uncushioned pupillary area of the anterior cortex. This would account for the radial arrangement of the opacities. The edema present during the acute attack would account for the more intense whiteness during that time.

The diagnosis depends on accurate biomicroscopy with the slitlamp and microscope. Correct diagnosis has importance during an acute glaucomatous attack, since the opacities may be mistaken for exudate on the anterior capsule in the presence of marked corneal edema. This occurred in one of my cases. In two others, a diagnosis of capsular exfoliation had previously been made. All three of these patients were seen by me within a period of three weeks.*

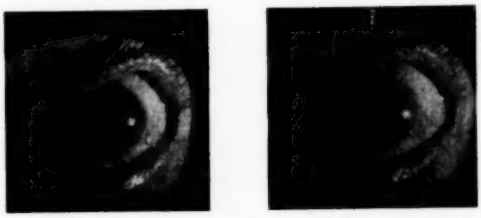

Fig. 2 (Sugar). Stereophotograph of subcapsular opacities in an eye that had suffered an attack of acute glaucoma.

Recognition of "Glaukomflecken" may also aid in establishing a definite diagnosis of previous acute glaucoma in an eye in which an acute attack has been completely relieved, as occurred in a case described by Weill and Hordman.[8] It would be possible also to recognize two or more previous attacks in the same eye, if the attacks were severe enough to cause the lens lesions, and if a sufficient time interval were to elapse between the separate attacks for new, clear, lens fibers to form.

Case reports

Case 1. A. K., a 50-year-old woman, was first seen by me in February, 1938. She stated that for a period of several months redness and aching of the right eye recurred in the late afternoon and after reading or seeing motion pictures.

* Since writing this paper, two additional cases of "Glaukomflecken" have been observed, one after an interval of five years following an acute glaucomatous attack; the second, a recent case which had previously been considered to be glaucoma capsulare.

One week before admission to the Illinois Eye and Ear Infirmary (February 21, 1938), the right eye had become red and painful and remained so. On admission, the visual acuity of the right eye was reduced to perception of hand movements; that of the left eye was normal. Tonometric readings were: R.E., 60 mm. Hg (Schiøtz); L. E., 19 mm. In spite of the intensive use of eserine, the intraocular pressure in the right eye could not be reduced satisfactorily. On February 25, 1938, an iridectomy was, therefore, performed. The tonometric readings thereafter always remained normal. The patient was followed by me for a period of three years and then again examined in April, 1946. Definite "Glaukomflecken" were present in the anterior cortex at a depth equal to about two thirds of the corneal thickness.

Case 2. J. K., a man, aged 44 years, was first seen by me in December, 1940. He had experienced severe pain in the right eye for the past five days. Treatment with miotics had been started on the third day but was ineffective. On admission to the Illinois Eye and Ear Infirmary (December 23, 1940), the tonometric reading for the right eye was 80 mm. Treatment with miotics continued to be ineffective. An iridectomy *ab externo* with incarceration of the iris was performed on the day following admission. The intraocular pressure remained normal thereafter. The patient was seen again in April, 1946, at which time typical "Glaukomflecken" were present in the anterior cortex at a depth equal to about two thirds of the corneal thickness.

These first two cases are cited to show the typical change in relative position of the lens opacities as time passes. In both of these cases, the depth of the opacities was approximately the same, equivalent to two thirds of the thickness of the corneal stroma near its apex.

Case 3. J. K., a woman, aged 50 years, was first seen at the Illinois Eye and Ear Infirmary on January 28, 1946. She complained of having had pain and redness of the right eye and severe supraorbital and temporal headache for the past three weeks, following a severe episode of influenza. The cornea of the right eye was steamy, the pupil dilated to 7 mm., and the tonometric reading was 57 mm. Hg (Schiøtz). After clearing of the cornea with glycerin, the anterior chamber was found to be very shallow. The aqueous was clear. Opacities in the region of the anterior capsule were interpreted to be capsular exfoliation. Some excavation at the upper temporal border of the disc was believed to be present. The left eye showed no evidence of capsular exfoliation nor lens opacities.

The patient was treated intensively with eserine without effect. An iridencleisis was successfully performed on January 30, 1946, at the Chicago State Hospital, where the patient was being treated for involutional melancholia. She was first seen by me two weeks later, at which time the right lens opacities were found to be typical cataracta glaucomatosa acuta.

Case 4. Mrs. E. S., aged 65 years, was first seen by me on February 28, 1946. Four weeks previously she had experienced slight attacks of blurred vision with slight aching around the left eye. One week later, a severe attack occurred and persisted. The right eye had been enucleated following similar attacks of blurred vision and subsequent antiglaucoma surgery. Vision in the left eye was 20/200, with and without correction. A caput-medusa type of conjunctival injection was present. The pupil was dilated and the anterior chamber was found to be shallow. "Glaukomflecken" were present. They had been interpreted as capsular exfoliation. The disc was normal. The

tonometric reading was 60 mm. Hg (Schiøtz). Intensive treatment with eserine was ineffective, so an iridectomy-iridencleisis was performed. The opacities on subsequent examinations showed less intense color but did not change significantly otherwise.

Cases 3 and 4 are interesting in that both had been previously diagnosed as capsular exfoliation. During the acute attack, the subcapsular position is, of course, difficult to ascertain, but the presence of changes in the center of the pupillary area is a pathognomonic sign of cataracta glaucomatosa acuta in contradistinction to capsular exfoliation.

Case 5. Mrs. A. H. M., aged 49 years, was first seen by me on February 22, 1946. Three weeks earlier, while vacationing in another state, she had awakened with severe headache. She was treated for nearly three weeks with atropine and penicillin. During the past three days, she had received eserine instead. Examination revealed a reduction of visual acuity in the left eye to perception of hand movements at 1 foot. The cornea was markedly steamy. Glycerin dehydration was ineffective in clearing the cornea. Pigment deposits were visible on the posterior corneal surface. The anterior chamber was only slightly shallow. Whitish spots appeared to be present on the lens capsule. In view of the history, I interpreted the hazy spots to be exudate. The tonometric reading with the Gradle-Schiøtz tonometer was 60 mm. Hg. Intensive treatment with eserine was instituted but was ineffective in reducing the intraocular pressure. An iridectomy-iridencleisis was done on February 22, 1946. Since then, the vision has returned to 20/25 with correction, and the tension has remained normal. The first postoperative examination revealed that the capsular spots were typical subepithelial lens opacities (fig. 1) of cataracta glaucomatosa acuta. These were less intense in color than during the acute attack. No evidence of primary uveitis was present.

Case 5 is an example of a mistake in diagnosis resulting from the presence of "Glaukomflecken." In this instance, the first oculist who saw this patient probably used atropine as a result of making the same mistake. Fortunately, the history of ineffective use of atropine for a relatively long period pointed out the correct treatment.

Case 6. Mrs. J. P., aged 59 years, was examined by Dr. S. J. Meyer on June 9, 1941. She was found to be 3.75 diopters hyperopic in each eye. Tonometric readings were: R.E., 24 mm.; L.E., 17 mm. Hg (Gradle-Schiøtz). An hour after instillation of euphthalmine for retinoscopy, the readings were: R.E., 22 mm.; L.E., 20 mm. No lens opacities were present. On April 10, 1946, she was seen by Dr. Meyer and me. She had had no ocular difficulty until 12 days previously, when she began to have headaches on the left side. Vision of the left eye was blurred. On the following day an antiglaucoma iridectomy was performed for acute glaucoma.

Upon examination, on April 10, 1946, large typical "Glaukomflecken" were found under the left anterior capsule. The tonometric reading in this eye was 22 mm. Hg (Gradle-Schiøtz).

Case 6 differs from the other three recent cases described in that the patient had symptoms only one day before surgical intervention. In the other three, the attack had lasted three or four weeks before intervention. It is, therefore, unlikely that a long period is required to produce the lens opacities. In many other cases of acute glaucoma with high tension, even those untreated for several weeks, no "Glaukomflecken" have been seen. The histories in the cases of traumatic "Glaukomflecken" indicate that a momentary

very high increase of intraocular pressure may be all that is required for their development.

In this case, the previous examination in 1941 revealed no pathologic condition of the lens, thereby indicating the relation between the acute episode and the presence of the lens changes.

Conclusions

Six cases of cataracta glaucomatosa acuta are reported together with a summary of the literature. The condition is important chiefly in differential diagnosis and in establishing the diagnosis of a previous attack of acute glaucoma.

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DETERMINATION OF OCULAR TENSION AND RIGIDITY IN RABBITS*

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Because of the insufficient data in the literature on the subject of this communication, it was deemed necessary to evaluate the normal range of ocular tension and rigidity in rabbits under varying physiologic conditions prior to experiments on changes of ocular pressure and tension.

There are two accepted methods of determining intraocular pressure; namely, the manometric and the tonometric. For purposes of comparative studies over a long period, the tonometric method was considered preferable.

Methods and Materials

Twenty rabbits of both sexes of New Zealand and Checkered Giant varieties, varying in age from one to two years, were used. Ocular tension and rigidity were ascertained by a Schiøtz tonometer which had been standardized at the New York checking station. The third corrected curve of Schiøtz was used.

The eye was anesthetized with one drop of 1-percent butyn. To ascertain ocular rigidity, tension was obtained with two weights, the 5.5-gram and the 10-gram. Whenever two readings with the two weights did not reveal significant differences, the rigidity was assumed to be normal. A higher tension with the 10-gram than with the 5.5-gram weight indicated an increase in rigidity; a lower tension, a decrease.

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* From Toledo Hospital Institute of Medical Research. This work was supported by a grant from the Snyder Ophthalmic Foundation.

† Research Ophthalmologist of the Snyder Ophthalmic Foundation.

During the first phase of the experiments, the normal values were determined over a period of three weeks. The second phase of the experiment consisted in instilling into the eyes a solution of 1-percent paredrine, 1-percent pilocarpine, and 1-percent atropine The drugs were introduced in single drops three times over a 15-minute period. The readings were made in 30 minutes and in four hours.

The third phase of the experiment consisted in the determination of ocular tension and rigidity by hypotonic (distilled water), hypertonic (4-percent saline), and isotonic (0.9-percent saline) solutions. These solutions were given by stomach tube in 40-c.c. volumes per kilogram of body weight. Readings were made over a period of four hours at 5- to 10-minute intervals.

Averages and standard deviations were evaluated in all experiments. Application of the following formula determined whether the findings obtained in the various experiments were significant. Differences were considered significant when they were larger than $3\sqrt{SE_{Mx}^2 + SE_{My}^2}$.

SE—standard error of the distribution of the magnitudes.

M—arithmetic mean.

x—varying abscissal value.

y—varying ordinate value.

TABLE 1

NORMAL OCULAR TENSION IN MM. HG AND RIGIDITY IN RABBITS

No. of Rabbit	Right Eye		Left Eye	
	5.5-gm. Weight	10.0-gm. Weight	5.5-gm. Weight	10.0-gm. Weight
61	29±4	27±4	27±3	27±2.5
196	24±3	25±5	23±2	24±4.0
225	24±3	23±4	22±3.5	23±4.5
242	26±3	26±4.5	26±4.5	25±3.0
243	24±3	27±3.5	23±3	26±2.5
255	27±5	23±5	23±3.5	21±3.5
291	30±5	34±6	26±2.5	30±3.0
293	27±4	28±4	26±2.5	27±2.5
315	20±3	20±4	18±1	16±2.0
316	19±1	20±2.5	19±1	20±1.0
351	20±5	24±5	24±2.5	20±5.0
369	26±4	29±3	25±3	29±3.0
370	25±4	27±4	20±2	24±3.0
371	28±4	30±6	28±4	31±4.0
372	27±4	27±4.5	24±3	27±5.5
373	25±4	27±3	24±2	26±4
374	27±4	26±4	26±4	27±3
375	23±4	23±3	20±1.5	23±4
376	22±4	22±4.5	21±4	22±4
377	20±4	17±2	21±4	18±5

RESULTS

The ocular tension with the 5.5-gram weight varied in 20 rabbits between 18 and 30 mm. Hg. The standard deviation for each animal varied from 1 to 5. For

TABLE 2

EXAMPLES OF DAILY DETERMINATIONS EXPRESSED IN MM. HG OF TONOMETRIC OCULAR TENSION IN TWO RABBITS

Day	Rabbit No. 243				Rabbit No. 225			
	Right Eye		Left Eye		Right Eye		Left Eye	
	5.5-gm. Weight	10.0-gm. Weight	5.5-gm. Weight	10.0-gm. Weight	5.5-gm. Weight	10.0-gm. Weight	5.5-gm. Weight	10.0-gm. Weight
1	25	24	25	24	29	24	25	27
2	25	27	21	24	21	20	21	20
3	21	27	21	27	20	27	23	31
4	25	24	27	22	25	20	21	24
5	21	27	21	25	20	20	27	24
6	20	25	23	27	29	20	25	18
7	21	22	18	24	21	20	25	20
8	23	24	21	24	25	29	21	27
9	29	36	29	26	25	25	25	24
10	23	27	23	27	25	27	18	19
11	25	31	25	29	23	20	18	19
12	29	31	27	31	25	20	18	20

TABLE 3

EFFECTS OF VARIOUS DRUGS ON OCULAR TENSION IN MM. HG AND RIGIDITY OF RIGHT EYE OF RABBITS

No. of Rabbit	Paredrine 1%				Pilocarpine 1%				Atropine 1%			
	5.5-gm. Weight		10.0-gm. Weight		5.5-gm. Weight		10.0-gm. Weight		5.5-gm. Weight		10.0-gm. Weight	
	30 min.	4 hrs.	30 min.	4 hrs.	30 min.	4 hr.	30 min.	4 hrs.	30 min.	4 hrs.	30 min.	4 hrs.
61	32 ±3.5	27 ±5.5	35 ±4.0	31 ±6.0	33 ±2.5	31 ±2.2	33 ±6.0	33 ±5.5	33 ±4.0	32 ±4.0	35 ± 7.0	29 ±6.0
196	24 ±2.5	22 ±4.5	27 ±3.0	21 ±3.5	24 ±2.5	23 ±1.5	25 ±5.0	26 ±2.5	28 ±6.0	24 ±4.0	22 ± 6.0	25 ±2.5
225	24 ±3.5	20 ±2.0	24 ±3.5	20 ±2.0	25 ±2.0	21 ±1.5	22 ±4.0	22 ±2.5	26 ±5.0	26 ±6.0	25 ± 6.0	22 ±2.5
242	30 ±2.0	24 ±4.0	31 ±5.6	26 ±5.0	29 ±2.0	26 ±4.0	34 ±5.0	28 ±3.5	27 ±2.5	26 ±3.5	32 ± 7.5	26 ±7.5
243	29 ±5.0	24 ±5.0	28 ±5.0	27 ±5.0	29 ±3.0	26 ±2.0	32 ±4.0	27 ±4.0	29 ±3.0	29 ±2.5	27 ± 8.5	28 ±2.5
255	30 ±2.5	24 ±3.0	30 ±4.0	28 ±2.5	24 ±5.5	27 ±4.0	25 ±5.0	29 ±7.5	26 ±7.5	27 ±3.5	22 ± 6.0	26 ±4.0
291	36 ±4.0	30 ±2.0	38 ±4.5	31 ±4.0	34 ±6.0	35 ±3.0	39 ±5.0	34 ±5.5	33 ±3.5	32 ±3.0	34 ±10.0	39 ±7.5
293	32 ±3.0	31 ±3.5	35 ±5.0	32 ±2.0	32 ±8.0	36 ±4.0	30 ±5.5	34 ±4.5	31 ±7.0	29 ±3.5	29 ± 7.0	28 ±5.0
315					23 ±2.0	18 ±0.0	22 ±6.0	22 ±1.0	24 ±2.5	23 ±2.5	23 ± 3.5	20 ±1.5
316					23 ±3.0	21 ±4.0	21 ±4.5	24 ±6.0	24 ±4.5	27 ±4.0	23 ± 4.0	24 ±5.5

the 10-gram weight, the tension was from 20 to 34 mm. with a standard deviation of 2.5 to 6 (table 1). There was no essential difference in the tensions between morning and afternoon determinations. It was noted that the more excitable rabbits were prone to greater variations in tension. There were no significant differences in the results for the two different weights (table 2).

Instillation of 3 drops of 1-percent paredrine in the eyes of eight animals showed an ocular tension varying from 24 to 36 mm. with the 5.5-gram weight and 24 to 38 mm. with the 10-gram weight. Although the average readings appear higher than without paredrine, the majority of animals showed no significant changes either in tension or in rigidity. Introduction of pilocarpine and atropine was equally without appreciable changes (table 3).

Oral administration of isotonic, hypotonic, and hypertonic solutions showed significant changes. Following the use of hypotonic solutions, there was an increase in tension in 10 to 15 minutes. The rigidity remained unchanged. The difference in tension from the normal values varied from 6 to 14 mm. Hg. Isotonic solutions induced no significant changes. Administration of hypertonic solution resulted in a decrease of tension but without change in rigidity. The decrease occurred within 15 minutes and was less than normal by 6 to 10 mm. Hg (table 4).

DISCUSSION

The choice of method of estimating ocular tension in experimental animals depends on the purpose of the investigation. The manometric procedure produces variable degrees of trauma which may influence the experiment, and the number of determinations is necessarily limited. The advantage lies in obtaining absolute values. The tonometric method, on the

TABLE 4

OCULAR TENSION OF THE LEFT EYE BEFORE AND AFTER ORAL ADMINISTRATION OF ISOTONIC, HYPOTONIC, AND HYPERTONIC SOLUTIONS

No. of Rabbit	Distilled Water				.9% NaCl				4% NaCl			
	5.5-gm. Weight		10.0-gm. Weight		5.5-gm. Weight		10.0-gm. Weight		5.5-gm. Weight		10.0-gm. Weight	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
315	19	33	20	31	19	21	24	20	18	10	20	8
316	19	29	18	27	21	21	20	24	19	11	19	15
369	25	31	29	39	25	27	31	33	21	15	22	11
373	20	27	23	31	21	23	24	24	20	11	20	13
375	21	33	24	36	20	21	21	24	19	9	19	9

other hand, allows repeated determinations without inflicting injury. It must be emphasized that the method measures the impressibility of the wall of the eye from which tension is deduced. If comparative values are desired to determine experimental changes, the tonometric procedure is adequate. However, the standard deviation should be ascertained to avoid ascribing undue significance to all variations. To obtain comparative values, a sufficiently large number of determinations must be made, the averages determined, and standard deviations calculated.

Gruenhagen's[1] manometric determinations of the rabbit's ocular tension varied between 25 to 26.5 mm. Hg. The range of tonometric readings in our experiment was from 20 to 30 mm. These readings also agree with results obtained in man.[2, 3, 4] In the normal human eye, there is a diurnal variation,[5, 6] frequently of 5 to 6 mm. Hg. The tension is greatest in the morning and falls gradually during the day. It begins to rise again at night. It was noted that the difference in the morning and afternoon tension in the rabbit was not significant.

In evaluating the findings in these experiments, the results of Friedenwald's tonometric studies[7] were employed. Two different weights were used. When similar readings were obtained with the two weights, the rigidity was considered normal. Friedenwald's definition of the term, rigidity, is the resistance which the eye exerts to distending forces.

The action of atropine and eserine on ocular tension has been ascertained by other investigators.[8] Their results indicated that by the use of manometric methods there were no significant changes. Slight deviations found by other workers[9]

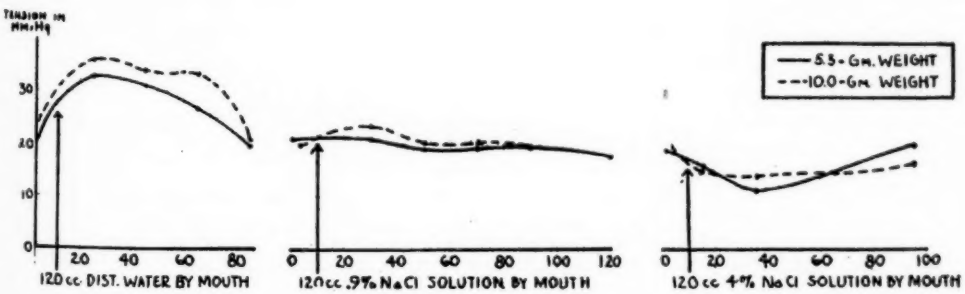

Chart 1 (Schmerl and Steinberg). Examples of changes in ocular tension of the left eye of a rabbit before and after oral administration of isotonic, hypotonic, and hypertonic solutions.

may be accounted for by conditions in the experimental procedures, such as partly filled anterior chambers.

Drinking of water tends to raise the ocular tension, and the Marx test is an application of the phenomenon. Studies utilizing the "drinking test" indicated that relatively small volumes of water are capable of increasing the tension in the normal eye[10] and the more so in the glaucomatous.[11] On the basis of such experiments, it was postulated that osmotic pressure does not play a part in the elevation of the ocular tension. It was also pointed out[12, 13] that after introduction of hypertonic salt solution, the blood volume tends to return to normal within 30 minutes, whereas the ocular tension remains decreased for several hours. The physicochemical reactions involved in this process are not clearly understood.

In the experiments reported here, it is apparent that a certain relationship exists between salt concentration and ocular tension. With ingestion of hypotonic solutions, the tension is increased; with hypertonic, it is decreased; and with isotonic, there are no significant changes.

Summary

Tonometric determinations of the impressibility of the wall of eyes were made in a number of rabbits over a prolonged period. The tension and the rigidity were then deduced. Determinations were made at different periods of the day, after instillation of paredrine, atropine, and pilocarpine, and after ingestion of isotonic, hypotonic, and hypertonic salt solutions. Average values, standard deviations, and significant differences were determined.

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THE AUTONOMIC NERVOUS SYSTEM IN OCULAR DISEASES*

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It is the purpose of this thesis to present certain clinically studied ocular disturbances both functional and organic, which have as their common etiology dysfunction of the autonomic nervous system.

Recent knowledge of the role played by the autonomic nervous system in the functioning of the body has opened new vistas. The mechanisms are known by which pain, cold, emotional states, and other conditions that excite autonomic discharges can induce or participate in pathologic processes. Morbid phenomena which have long been inexplicable are thereby reasonably explained.

The borderline between normal and abnormal physiology and between functional and organic diseases is nowhere so thin as in the effects produced by dysfunction of the autonomic nervous system.

Those champions of the modern concept "Psycho-somatic medicine," such as Dunbar,[1, 2] and Weiss and English,[3] have found their best and most readily provable arguments in the study of the organic pathology resulting from autonomic imbalance. Actual structural change in the cells consistent with organic disease processes will be seen to follow prolonged physiologic upsets.

Subjective symptoms of functional origin are found giving rise to the objective signs of disease.

There are, perhaps, few places in the body so well adapted to the clinical study of such phenomena as the eye, much of whose normal physiology is under autonomic control.

ANATOMY

In the history of the investigation of the vegetative nervous system, anatomic knowledge developed far ahead of physiologic experiment.

Relatively little still is known of the central connections of the sympathetic-nervous-system fibers in the brain. On the basis of clinical and experimental studies, however, it is conjectured that such centers probably exist in the cerebrum, the hypothalamus, the medulla, and the cord (Beattie *et al.*,[4] 1930).

Evidence of cerebral control (especially the frontal lobes) over the sympathetic fibers of the eye is slight, but stimulation of a center immediately lateral to the infundibulum in the hypothalamic region brings about a pupillary dilatation, separation of the lids, and retraction of the nictitating membrane (Beattie,[5] 1935). This effect persists after section of nerves II, III, and V, but is stopped by destruction of the sympathetic. The general vasomotor centers are situated in the medulla. An "inferior ciliospinal center" for sympathetic control of the eye undoubtedly exists in the upper part of the cord between the levels of VI C and IV T.

Arising in the intermedio-lateral tract of the gray matter of the ciliospinal center, the preganglionic sympathetic fibers leave the central nervous system by the ventral roots of the thoracic nerves I, II, and III, with the larger number of fibers to the eye in the first thoracic root. The white rami communicantes continue the

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course of these fibers up the cervical-sympathetic chain, through the inferior and middle cervical ganglion to their termination in the superior cervical ganglion.

The majority of the nonmedulated, postganglionic fibers leave the superior cervical ganglion as the nervous caroticus internus, which accompanies the carotid artery through the carotid canal into the skull, where it breaks up into a fine plexus adherent to the vessel wall. This is divided into the internal carotid plexus and the cavernous plexus.

From the cavernous plexus, branches are given off to the third nerve, to the fourth nerve, to the Gasserian ganglion, and the first division of the fifth nerve, and thence to the eye by way of the long ciliary nerves, to the ciliary ganglion, and thence to the eye as vasomotor fibers via the short ciliary nerves.

From the carotid plexus branches are given off to the sixth nerve, to the branches of the ophthalmic artery, and to the periorbita, the muscle of Müller, and possibly the lacrimal gland.

The parasympathetic nervous system of the eye is found in association with the third nerve, in which are found the pupillo-constrictor fibers to the iris and the nerves to the ciliary muscle, relayed to their end stations by way of the short ciliary nerves (Duke-Elder[6]).

For a comprehensive review of the autonomic innervation of the eye, reference is made to Kuntz[7] and White and Smithwick.[8]

Physiology

For our purposes, a consideration of the physiology of the autonomic nervous system will be limited to a brief review of its ocular relationships with particular emphasis on vasomotor control in the eye.

A great part of the work which has led to our present understanding of the physiology of the sympathetic nervous system has been carried out by Cannon[9] and summed up in his book, "The Wisdom of the Body." He particularly emphasized the essential character of the system in conditions of stress and strain. This applies to the eye no less than it does to other parts of the body. Some of the more common conditions which arouse its activity are pain, extremes of temperature, lack of oxygen, infection, and intense emotional or psychic trauma. He has stated that this mechanism may actually be harmful unless the emotion is transformed into action. "If no action succeeds the excitement and the emotional stress (even worry or anxiety) persists, then the bodily changes due to the stress may be profoundly upsetting to the organism as a whole" (Cannon,[10] 1933). This same point has been expressed by Fulton[11] in the statement that "the heart and circulation may be worked just as hard from an armchair as from a rower's seat."

Just as anatomic investigation has demonstrated the importance of the hypothalamic region in the autonomic nervous system, so physiologic experimentation has shown that the hypothalamus, in addition to carrying out the autonomic expression of emotion, serves as a regulator of body temperature, through vasomotor control, and the whole delicate involuntary adjustment to the external environment. Alvarez[12] has presented convincing evidence that the hypothalamus can be upset by fatigue, lack of sleep, and nervous strain, and that, in many persons, it behaves erratically because of poor nervous inheritance

Of all functions of the autonomic nervous system, that of the vasoconstrictor action of the sympathetic is of most interest to the ophthalmologist. In addition to distributing vasoconstrictor fibers to

the entire surface of the body, the sympathetic system constricts the cerebral and retinal arterioles (Penfield,[13] 1932).

While the most active vasoconstrictor action supposedly takes place in the arterioles, a definite nervous control of the capillaries and veins has also been demonstrated. Cessation of blood flow through a capillary loop results from constriction of the Rouget cells and swelling of the endothelial-cell nuclei and follows a stimulus with too short a latent period to be anything but nervous action. Nervous control of the veins has also been demonstrated, and there is good reason to believe that the engorgement of the veins after sympathectomy is due to their release from the vasoconstrictor center.

Because the control of the entire circulation is essentially directed to regulate the blood supply to the capillaries, they are the vital part of the circulation. This is especially true of the eye and most particularly true of the macular area of the retina, whose metabolic interchange is wholly through the underlying choriocapillaris.

The contractility of the arterioles, capillaries, and venules of the eye, as elsewhere in the body, is controlled by two mechanisms, a nervous and a chemical, by the reciprocal action of which the small vessels are constantly kept in a state of tonicity. Reference has been made to the physiology of nervous control. Chemical control is maintained more directly by local conditions and forms a fine adjustment of great precision, though there is a close interrelation between the two.

The chemical control of the circulation is carried out by two groups of substances: the first, hormonal and acting as constrictors and typified by pituitrin and adrenalin; and the second, produced locally by the tissue cells and typified in histamine. The complete reaction produced by these histamine-like substances is a "triple response," consisting of a primary and local dilatation of the minute vessels, a local increase in capillary permeability, and a widespread dilatation of neighboring arterioles. The occurrence of this reaction in the vascular system of the inner eye will be shown to be of considerable importance. Recent experiments by Shorr *et al.*[14] have demonstrated the production by the kidney of a vaso-excitor material, probably identical with the renin-angrotonin system in its action on the terminal vascular bed, and an opposite-acting, vaso-depressor material produced by the liver and skeletal muscle whose genesis is anoxia in tissues.

Method of study

The various clinical methods of study of vasomotor pathways and reactions have been well described by White and Smithwick[8] and Kuntz.[7] Reference is made primarily to peripheral vascular disturbances in the extremities, but the methods used are equally applicable to the study of ocular vasomotor disturbances. These methods have been augmented by observation on certain objective and subjective ocular signs and symptoms indicative of autonomic imbalance and their relationship to the clinical entity of "vasoneurotic diathesis" described by Hornikker[15] and by Gifford and Marquardt.[16]

Due to lack of facilities, complete studies were carried out on relatively few of the cases presented in this paper. However, it became possible through observation of these cases to recognize a symptom complex in the others, which, when associated with certain typical signs of vasomotor instability, was sufficiently characteristic almost to preclude the necessity of pressor tests, skin-temperature readings, capillary microscopy, diagnostic procaine block, and foreign protein test.

THE AUTONOMICALLY UNSTABLE PERSON

The complete picture of the "typical" autonomically unstable individual, as seen in great numbers in the military forces of the United States, is as follows: An asthenic young man, about 22 years of age, rather nervous and ill at ease during questioning and examination, with from 9 to 18 months' training and about 7 months of overseas duty or at some rather isolated mainland post. He complains of frequent or constant headache, usually unilateral and frequently retrobulbar in location. He often has transient dizziness or syncope associated with blurring of vision which may last from a few seconds to 10 minutes. The visual disturbance varies from a slight "film" to complete "blackout." The patient states that he has lost some weight, often as much as 20 pounds; that he has always been "nervous" but that in recent months he has become more so and he has had insomnia. He sometimes volunteers the information that he thinks this nervousness is due to "too much smoking" or vice versa, that he is smoking much more lately because of his nervousness. In any case, he has often doubled his cigarette consumption. If he has been in active combat, he readily admits to being very anxious and emotionally upset immediately preceding, sometimes during, and after action. If he is married, which is usually the case, he confesses anxieties about his wife, his children, his farm crops, or his domestic problems in general. Nostalgia is a frequent complaint.

When questioned about his family, there is frequently a history of an ailing mother with "sick headaches." There is usually a fairly stable family background with little abnormal parental behavior.

Physical examinations (aside from the various ocular signs to be described later) shows a rather tall, thin, under weight young man. Hands and feet are moist to actually wet with perspiration regardless of the climatic conditions prevailing at the moment of examination. (Some men were examined in the northwestern United States in winter and others in the tropics with high temperatures and humidity.) The fingers and toes are cold to touch. The finger tips become quickly more cyanotic than normal, when held hanging at the sides, and very pale when elevated for a few minutes above the head. The pupils are dilated in an ordinarily light room but respond readily to light and accommodation. The blood pressure is an average 120/70 and is affected very little if at all by pressor test. The pulse is inclined to be more rapid than normal in a resting person. General physical examination, including a thorough search for any possible foci of infection, is negative except for the occasional finding of a granuloma at the apex of a devitalized tooth and occasional hypertrophied tonsils.

There is a fine tremor of the extended hands, at times very marked. Psychiatric evaluation, which was obtained in a fairly large number of cases, revealed tendencies toward, or frank and outspoken anxiety neurosis. Several soldiers showed many of the signs and symptoms of "combat fatigue," and in a few instances, the autonomic instability was so marked as to make the diagnosis of true "combat fatigue" open to question.

The military duty to which these men were subjected varied tremendously. Some had had most difficult and prolonged combat duty with days and weeks of exposure to battle conditions. They had lived in muddy fox holes in temperatures well over 100°F., with humidity of 80 to 90 percent. Food had been mostly C and K rations. Sleep was fitful because of constant alerts. They had endured in-

cessant bombing and heavy shell fire and, although they had suffered no physical injury of any consequence, had been subjected to intense psychic trauma. Others had had prolonged periods of time. There were numerous instances in which the only rigors of military duty were those found in "boot camp" or indoctrination schools and training centers. For the most part, these men were very young,

TABLE 1

CENTRAL ANGIOSPASTIC RETINOPATHY—SYMPTOMS

Case No.	Headache	Corrected Vision		Scotoma 2/2,000	Metamorphopsia	Variation in Vision	Sensitivity to Cold	Cyanosis of Hands	Pallor of Hands	Hyperhydrosis	Cold Hands	Nervousness	Cigarettes per Day
		O.D.	O.S.										
1	Left Frontal	20/20	20/200	1°	no test	2+	1+	1+	1+	2+	2+	1+	20
2	Bilateral Orbital	20/50	20/50	no test	no test	3+	2+	2+	2+	3+	2+	1+	15
3	Orbital	20/20	20/30	1°	no test	2+	1+	2+	2+	3+	2+	2+	20
4	Frontal	20/50	20/50	½°	2+	3+	1+	1+	1+	2+	2+	1+	10
5	Orbital	20/25	20/25	½°	2+	4+	—	1+	1+	2+	1+	—	15
6	None	20/40	20/20	1°	2+	—	1+	1+	1+	2+	—	—	15
7	Orbital	20/40	20/20	2°	3+	—	—	no test	no test	1+	1+	—	10
8	Frontal	20/30	20/30	no test	no test	3+	1+	2+	2+	3+	2+	2+	0
9	Orbital	20/30	20/40	1°	1+	2+	—	1+	1+	2+	2+	2+	10
10	None	20/80	20/20	2°	no test	—	—	no test	no test	1+	1+	—	20
11	Orbital	20/100	20/20	3°	2+	—	1+	2+	2+	2+	2+	—	10
12	Orbital	20/30	20/20	½°	2+	3+	2+	—	—	3+	2+	3+	40
13	Frontal	20/30	20/30	no test	no test	3+	1+	1+	1+	2+	1+	2+	20
14	None	20/40	20/20	5°	no test	—	—	no test	no test	3+	2+	—	0
15	Orbital	20/20	20/20	none	none	3+	—	no test	no test	3+	1+	3+	30
16	Frontal	20/20	20/20	none	none	2+	—	no test	no test	1+	1+	1+	10
17	Orbital	4/200	20/20	25°	no test	—	—	1+	1+	2+	1+	2+	20
18	Orbital	20/20	20/80	1°	2+	3+	1+	2+	2+	4+	2+	2+	30
19	Frontal	12/200	20/20	2°	no test	2+	—	1+	1+	2+	2+	3+	30
20	None	20/20	20/70	3°	3+	2+	—	1+	1+	2+	2+	—	10
21	Frontal	20/30	20/30	½°	no test	4+	1+	0	0	3+	2+	3+	25
22	Right Orbital	20/60	20/20	1°	2+	3+	3+	2+	2+	2+	3+	2+	30
23	Right Orbital	20/200	20/50	3° O.D. 1° O.S.	no test	0+	1+	3+	3+	4+	3+	4+	0
24	Orbital	20/40	20/40	½°	no test	2+	0	2+	2+	3+	3+	3+	0
25	Frontal	20/200	20/20	3°	2+	3+	0	2+	3+	4+	2+	4+	40
26	Orbital	20/30	20/20	1°	1+	2+	0	2+	3+	3+	3+	1+	20
27	LeftOrbital	20/20	20/30	1°	2+	2+	1+	3+	3+	4+	3+	2+	10
28	None	20/25	20/25	0	2+	3+	0	2+	3+	3+	2+	1+	20
29	Frontal	20/40	20/20	1°	2+	2+	2+	2+	3+	4+	2+	2+	0
30	Orbital	20/40	20/20	2°	no test	2+	0	3+	3+	4+	3+	2+	30
31	Orbital	20/50	20/40	2°	2+	1+	1+	3+	2+	3+	3+	2+	0
32	Orbital	20/70	20/30	2° O.D. 1° O.S.	1+	2+	1+	2+	3+	3+	3+	2+	20
33	Frontal	20/40	20/40	1°	2+	2+	0	1+	1+	3+	2+	1+	20
34	None	20/30	20/25	0	1+	2+	3+	2+	4+	3+	4+	1+	15
35	Right Orbital	20/100	20/20	2°	2+	1+	3+	1+	2+	2+	3+	2+	40
36	Right Orbital	20/200	20/20	5°	2+	3+	3+	3+	3+	4+	4+	3+	60
37	Frontal	20/40	20/40	no test	no test	2+	2+	1+	2+	3+	3+	1+	20
38	Frontal	20/70	20/40	5°	1+	2+	2+	2+	2+	3+	3+	2+	15
39	Orbital	20/30	20/30	1°	2+	3+	0	2+	2+	3+	3+	3+	0
40	Orbital	20/30	20/20	½°	0	2+	0	2+	3+	4+	3+	0	25

duty in isolated outposts such as the Aleutian Islands, where their chief enemy was lack of activity and exquisite boredom. They were repeatedly exposed to subzero weather and, in several instances, suffered greatly from it. Some had suffered from intense glare of the tropic sun on water and attributed their ocular disturbances to this glare, whereas others, including several submariners, were denied the sight of the sun for weeks at a were frankly, miserably homesick. Their psychiatric examinations showed almost uniform tendencies toward true anxiety neuroses.

It will be seen from analysis of the foregoing data that all of these patients had two things in common: They demonstrated the clinical picture of vasoneurotic diathesis, and they were all subjected to one or more known autonomic nervous-system stimulants; namely, emotional or

psychic trauma, exposure to extremes of temperature, the vasospastic action of cigarettes, occasional infection, pain, dehydration and hypoglycemia induced by prolonged periods of strenuous muscular exertion, and fatigue approaching exhaustion.

Certain other cases will be discussed in which it was felt that the ocular disturbances were the result of direct trauma to the eye, as in contusion or exposure to infrared or heat rays, both of which are known to give rise to histamine production with the resulting "triple response" in the tissues involved.

Ocular manifestations

The ocular manifestations of autonomic-nervous-system dysfunction to be considered are as follows: (1) central angiospastic retinopathy; (2) ocular changes in Raynaud's disease; (3) amaurosis fugax; and (4) commotio retinae.

Central angiospastic retinopathy

This is the term applied by Gifford and Marquardt[16] to a type of macular retinal lesion which they felt to be definitely of circulatory origin and of sufficient importance to be considered a clinical entity.

It is my opinion that their conclusions and the name were well supported by their case reports. My own case reports will be seen to confirm their findings in many respects. As pointed out in their article, the identical clinical picture has been described at intervals in the literature under the names: recurrent central retinitis; retinitis centralis; central serous retinopathy; preretinal edema; idiopathic flat detachment of the retina; retinitis centralis annularis; central angiospastic retinitis; angiosclerotic and angiospastic retinoses; juvenile exudative macular retinitis; and choroiditis centralis serosa.

In the majority of reports, small groups of cases were seen and, for the most part, the investigators considered the condition of inflammatory origin. A notable exception to this was the suggestion of Kraupa[17] that the lesions could be attributed to retinal ischemia resulting from capillary changes. It remained for Horniker,[15] and later for Bailliart,[18] and Gifford and Marquardt[16] to establish evidence of vasomotor instability in these cases and to demonstrate the vasospastic etiology of the retinal lesion.

Shortly after the entrance of the United States into World War II, medical officers in the United States Navy began to see cases of binocular or monocular macular lesions in young people, in numbers out of all proportion to those seen in civilian practice in the same age group. The cases appeared with such regularity, and so many widely scattered officers commented upon them, that a study of the condition was requested by the National Research Council, Subcommittee of Ophthalmology, and was undertaken by Dr. F. C. Cordes.[19]

His preliminary report was based upon data furnished by 11 Naval medical officers stationed in Pacific Naval hospitals, supplemented by personal observations of a few cases. Data on approximately 16 cases for this report were submitted by me, and I was in frequent communication with Cordes during its preparation.

From a close study of my own cases and of the description of the cases submitted by the other medical officers and by Cordes, it is obvious that all were concerned with the same clinical entity. Furthermore, these cases fit perfectly the description which Horniker, and Gifford and Marquardt give of the lesion which they call "central angiospastic retinopathy," and which Duke-Elder[20] calls

TABLE 2

CENTRAL ANGIOSPASTIC RETINOPATHY—OPHTHALMOSCOPIC EXAMINATION

Case	Eye	Edema	Pigment Change	Foveal Reflex	Hole in Macula
1	O.S.	Early gray edema, macular halo	Granular pigment, late	Absent	Small, oval, deep
2	O.U.	Macula hazy, halo	Coarse granular	Absent	None
3	O.S.	Dull gray, faint	None	Absent	None
4	O.U.	Entire macula elevated	Fine pigmentation	Absent	None
5	O.U.	Marked gray edema	None	Absent	None
6	O.D.	Gray edema, bright halo	Granular pigment	Absent	Minute hole
7	O.D.	Very slight	Heavy granular	Absent	Small, deep, red
8	O.U.	Both maculas blurred	Coarse granular	Absent	None
9	O.U.	Perimacular edema, halo	Fine pigment, yellow dots	Absent	None
10	O.U.	None	Fine pigment	Absent	Small, sharp, red
11	O.D.	None	Fine pigment	Absent	Small, sharp edges
12	O.U.	Gray elevation, halo	Coarse mottling	Absent	None
13	O.U.	Marked gray edema	Fine granular	Absent	Small, red, sharp
14	O.D.	Blurred gray macula	Suggestion, fine white dots	Absent	None
15	O.U.	None	Faint, pigment change	Absent	None
16	O.D.	None	Coarse granular, marked	Absent	Sharp, small, red
17	O.U.	Marked, bright halo	Coarse granular	Absent	None
18	O.S.	Slight, early	Fine granular	Absent	Hole $\frac{1}{4}$ disc diameter
19	O.U.	None	Coarse, 5–6 yellow dots	Present	None
20	O.S.	None	Faint, fine pigment	Present	Minute, vertical oval
21	O.D.	Early edema, ring reflex	Granular with yellow dots	Absent	None
22	O.D.	Slight	Fine granular	Absent	Minute red hole
23	O.D.	Early slight edema	Coarse, mottled	Absent	Small, dark red hole
24	O.U.	Blurred, gray maculae	Fine, numerous yellow dots	Absent	None
25	O.D.	Slight grayness	Coarse, granular	Absent	Minute red, oval hole
26	O.D.	None	Fine	Absent	Minute red hole
27	O.S.	None	Slight	Absent	Minute, sharp hole
28	O.U.	Gray elevation macula	Fine	Absent	Small, sharp edges
29	O.D.	None	Heavy, coarse	Absent	Dark, sharp edges
30	O.D.	Slight	Coarse, granular	Absent	Small, oval, red
31	O.U.	Marked in early stages	Heavy, with yellow dots	Absent	Small mound with crater
32	O.U.	None	Faint	Absent	Small, sharp, round
33	O.U.	Marked in early stages	Early, moderate	Absent	Extremely small
34	O.U.	Slight	Coarse, granular	Absent	Irregular, small, right
35	O.D.	Gray, bright halo reflex	Fine, many yellow dots	Absent	Minute, oval, red
36	O.U.	Marked in early stages	Pear shaped, heavy	Absent	Mound with crater
37	O.U.	None	Moderate, some white dots	Absent	Round, sharp, red
38	O.D.	Slight	Many yellow dots	Absent	Small, crater like
39	O.U.	Slight	Coarse, many yellow dots	Absent	None
40	O.U.	Gray, small in area	Coarse, marked	Absent	Very small

"central serous retinopathy" in his textbook discussion of macular capillary disturbance.

For purposes of clarity and simplification, one case only will be reported in detail with results of examination of the peripheral vascular and autonomic nervous systems. The remaining 39 cases will be reported in tabular form. It is unfortunate that in this investigation facilities were not at hand with which accurate measurement could be made of skin-temperature changes; but, in the majority of instances, the changes were so marked as to be readily measured with relatively crude methods and, as mentioned above, the clinical manifestations were so marked in many instances as almost to preclude the necessity of special vasomotor tests.

CASE REPORT

J. D. S., a corporal, U. S. Marine Corps Reserve, aged 22 years, entered

the hospital on November 29, 1944, with a diagnosis of amblyopia. His trouble began in early June, 1944, while aboard a ship approaching Saipan, preparatory to invasion. He first noticed a very severe, constant "boring" type of right-sided headache which centered mostly in the right orbit and was not relieved by sleep or aspirin. A short time later he noticed a blurring of vision which at first occurred in "waves" and would then clear. This rapidly became more constant until vision was very poor most of the time. He stated that he was extremely nervous but "no more frightened than the rest of the fellows—which was plenty." During the long sea voyage, he had increased his cigarette consumption from 15 to 45 or 50 a day—mostly "because of nervousness and nothing to do." He also noticed marked photophobia but considered this natural from the glare on the water.

During the amphibious attack on the island, he was in one of the first "waves" ashore and was subjected to vigorous shell and small-arms fire and some very near misses and sharp blast concussions. His head continued to ache but was much worse during any lull in his activity. In the course of the next week, he was under almost continuous and very severe nervous tension, with little sleep or rest. Vision became so blurred in his right eye that he began shooting from his left shoulder, although at times there was noticeable blurring of the vision of the left eye.

He volunteered the information that for the past seven or eight years he had "never been able to depend on his right eye, which frequently blurred out, especially when he was under nervous tension or when it was very cold." For this reason, he did not report to sick bay, believing that the disturbance was temporary as it had been before. His home was in Wisconsin, and he had frequently noticed that he suffered more from the winter cold than most of his friends. He could not wear gloves because his hands "always got wet with sweat and then would freeze."

He carried on as best he could through the remainder of the invasion, reporting to the doctor because of his headache and poor vision only after his sector had been declared secure. Examination at that time showed vision to be 2/20 in the right eye, and a note was made in the health record that the "fundus details were indistinct and the retina seemed edematous." He was evacuated to a base hospital.

General physical examination showed a husky, well-developed young man who appeared well controlled and was very coöperative. There were no abnormalities in the system, and a thorough search for foci of infection including teeth, nose, and throat, and prostate were normal. X-ray studies of the chest were normal. Intradermal tuberculin test in 1:10,000 dilution was negative. Sedimentation rate was normal. Blood Kahn test was negative.

Patent clinical evidence of vasoneurotic diathesis was manifest as follows:

1. The pupils measured 8 mm. in diameter as compared with 2 and 3 mm. in two other enlisted men under the same lighting conditions.

2. The palms of the hands were grossly wet, so that, if a ruler edge were passed across them lightly, a pool of water collected in the center. This was in marked contrast with two normal control subjects.

3. Elevation of the hands above the head for three minutes produced a marked blanching of the fingers. When the hands were returned to shoulder level, they quickly showed a very blotchy appearance. This was noticed to a very mild degree in the controls.

4. With the hands hung dependent for three minutes, there was a noticeable cyanosis as compared with the controls.

5. The hands were cold to touch, especially the finger tips as compared to the controls'.

6. There was a considerable fine tremor of the extended hands.

7. The patient appeared calm but, when questioned about the tremor, stated that he always had it when he was "very nervous like I am now."

8. During the course of a rather short examination, the axillary perspiration soaked through and stained a large area of the shirt in marked contrast to the controls and the examiner in the same room.

Ocular examination. Vision in the right eye was 20/200 (2/20); left eye 20/20.

Visual field taken on the tangent screen at 2 M. with 2-mm. test object showed a 2° central scotoma, sharp in outline and dense, with the bulk of the defect extending below and nasal to fixation.

A test for metamorphopsia suggested by Comdr. Frank P. Smart[21] was positive to a marked degree in the right eye and suggestive, although not definite, in the left eye. The test consisted of having the patient fixate steadily a cross placed on the middle line of a music staff of five lines. He then drew the lines as he saw them. The two outer lines of the staff appeared to be bent outward from the fixation point, indicating an inward traction of the nerve elements of the macular area. This type of metamorphopsia was a very constant finding in most of the cases tested.

External examination of the eyes including cornea, iris, and lens was negative. The vitreous was clear. The macular area of the right eye showed a pear-shaped, granular, and pigmented lesion, with sharp edges approximately the diameter of two retinal-vein trunks. Around this the retina had a grayish tinge and showed a few faint radiating striations. There were five or six small yellowish dots in the area. The foveal reflex was absent. When the ophthalmoscope beam was cut down to a narrow slit, the central lesion appeared to be definitely depressed, and the surrounding retina slightly elevated, giving the appearance of a small crater at the top of a low mound. (A binocular ophthalmoscope was not available.)

The macula of the left eye showed an identical process except that it was of extremely slight degree and would have been missed entirely in a routine fundus examination. There was an irregular and eccentric foveal reflex and very little pigment change, but the central crater, although small, was definite, and was easily seen by red-free light.

Examination of the peripheral vascular system resulted in the following observations, in a draft-free room, at a temperature of 70°F. Skin temperatures were taken with a flat-bulb skin thermometer protected by a cork near its tip: (1) mouth temperature, 98.4°F.; (2) temperature of big toe, 83.2°F.; (3) temperature of middle finger, 87.2°F.; (4) temperature of big toe, three minutes after smoking one cigarette, 75°F.; (5) temperature of big toe after diagnostic procaine block of posterior tibial nerve behind the internal malleolus, right foot, 94.3°F.; (6) capillary microscopy of the bed of the nail showed a high degree of capillary narrowing.

A number of practically identical cases have recently been carefully studied both ophthalmologically and psychiatrically by Zeligs,[22] who approached the problem psychosomatically and pointed out the occurrence of anxiety (induced by combat) as a common-type factor in the production of central angiospastic retinopathy.

Retinal changes in Raynaud's disease

The following definition of Raynaud's disease was formulated by the peripheral vascular clinic of the Massachusetts General Hospital:

"Raynaud's disease is a form of peripheral vascular disturbance caused by tonic contraction of the smaller arteries in the extremities. During the early, uncomplicated states of the disease, there are no obvious pathologic changes in the walls of the arteries. The disease commonly involves symmetrical areas in the hands and feet, causing circulatory stasis with periods of cyanosis or pallid asphyxia. The severe cases go on to dry gangrene of the phalanges. The spasm is intermittent and occurs on exposure to cold or emotional stimuli; it involves only the terminal arteries while the main vessels continue their normal pulsations. Frequently these patients complain of excessive perspiration which is also limited to the extremities. The disease most commonly occurs in young individuals with hyperirritable nervous constitutions" (White and Smithwick[8]).

While the occurrence of the clinical entity described by Maurice Raynaud[23] is relatively uncommon, every student of peripheral vascular disturbances has encountered instances of acrocyanosis and all varieties and degrees of peripheral vasospasm. For practical purposes these may be assumed to be identical except in the intensity and duration of the spasm. Frequently these cases of mild vasospasm have been precipitated into typical Raynaud's disease. In true Raynaud's disease as well as in the borderline cases, hyperhidrosis is a prominent feature. This has also been seen to be a characteristic of the vasoneurotic diatheses almost universally associated with central angiospastic retinopathy.

Raynaud and others[24, 25, 26] have described attacks of intermittent constriction of the retinal vessels with blurring and even permanent loss of vision and Bailliart[27] has described a complete choroidal anemia with destructive retinal lesions. While it is true that a vasomotor neurosis would be expected to affect primarily the hands and feet, it is also true that the smaller arterioles (the site of the vasospasm) might well be affected in other parts of the body.

There is still some difference of opinion concerning the etiology of Raynaud's disease, but the greatest weight of evidence upholds Raynaud's original idea; namely, that at the onset of the disease the recurrent attacks of symmetrical vasospasm are due to an abnormal activity of the vasoconstrictor nerves.

I have had an unusual opportunity to study two cases of well-advanced Raynaud's disease in young men both of whom showed ocular disturbances. The cases were practically identical both in peripheral vascular involvement and in the eye examination. Skin-temperature readings were obtained in only one case, the report of which follows.

Case report

C. D. D., a 19-year-old yeoman, second class, was admitted to the hospital on the Dermatologic Service because of small, painful, dry ulcerations at the tips of the fingers and of several toes. He had first noticed pain and numbness of the hands, associated with extreme pallor of the fingers, when exposed to cold weather aboard a small ship in northern latitudes. While on this ship, he frequently was exposed to severe cold and active exercise and excitement in spite of his yeoman's rating, as each member of the crew was required to stand watches regardless of rate. He complained as little as possible for fear of being considered a shirker, but there were times when, under the combined stimulus of cold, exercise, and

excitement, the pain and discomfort were so intense as to cause him to weep. He particularly noted the prolonged, almost dead-white pallor of his fingers after these episodes. Several months before admission, he was transferred ashore, where he was assigned to work involving considerable typing. He was much more comfortable, but soon noticed that, after a few minutes of typing with his hands elevated to the typewriter keyboard at about the level of his nipples, the fingers became very pale and painful. He procured a high stool which lowered the level of his hands, and this helped for a while. During all this time, he had noticed that the small ulcerations on his finger tips failed to heal satisfactorily. His only ocular complaint was of periodic, somewhat disturbing blurring of his vision, especially in the right eye. These attacks would last for 5 to 15 minutes and were usually noticed when he was working under pressure to finish a piece of work in a specified time. He did not consider himself emotionally unstable nor nervous. He smoked 20 cigarettes a day.

Examination of his hands and feet showed typical symptoms of Raynaud's disease, including very wet, cold hands, and fingers that tapered almost to points, with symmetrical areas of dry gangrene and loss of substance at the tips, especially just under the nail edge. After three minutes' elevation of the hands to the level of the ears, they became extremely pale and began to give pain. On dependence of the hands to his sides, they quickly became very cyanotic. The same was true of the feet. The radial and dorsalis pedis pulses were well palpated.

TABLE 3

CENTRAL ANGIOSPASTIC RETINOPATHY—EXAMINATION OF THE PERIPHERAL VASCULAR SYSTEM

Case No.	Temp. of Toes Before Nerve Block	Temp. of Toes After Nerve Block	Mouth Temp.	Cigarette Reaction*	Capillar. Microscopy†
6	90.2°F.	95.4°F.	98.4°F.	8.4°F.	3+
12	82.4°F.	91.4°F.	98.6°F.	7.2°F.	2+
18	83.0°F.	90.2°F.	97.8°F.	9.0°F.	3+
21	88.6°F.	93.2°F.	98.6°F.	8.2°F.	2+
23	80.0°F.	88.8°F.	98.0°F.	6.4°F.	2+
25	80.2°F.	86.0°F.	98.2°F.	9.2°F.	4+
31	82.0°F.	90.0°F.	98.6°F.	7.2°F.	3+
35	86.4°F.	94.0°F.	99.0°F.	4.4°F.	3+
36	83.2°F.	Not taken	98.6°F.	8.2°F.	4+
39	84.0°F.	92.6°F.	98.4°F.	6.8°F.	3+

* Drop in temperature of big toe 3 minutes after finishing one cigarette.
† Spasm on basis of 1 to 4+.
Temperatures taken after 1 hour in a draft free room at 70°F.

Ocular examination. Vision was: R.E., 20/30 blurred; L.E., 20/15. Refraction with cycloplegic showed a plus 0.75D. sphere for each eye, but without change in vision. Ophthalmoscopic examination was negative in the left eye, but the terminal branches of the superior temporal artery of the right eye showed definite and marked vasospasm and irregularity of caliber near the macula. The macula of the right eye showed a rather coarse granular pigmentation, with loss of foveal reflex and a generally "smeared" appearance. There was no loss of substance in the fovea. The appearance of the macula was identical with the late stages of a typical mild case of central angiospastic retinopathy.

Skin temperature readings on the right foot were as follows: (1) room tempera-

ture, 70°F.; (2) skin temperature, knee, 79°F.; (3) skin temperature, base of big toe, 70°F.; (4) skin temperature, base of big toe after one cigarette, 65°F.; (5) skin temperature, knee, after procaine nerve block, 82°F.

During the preparation of the patient for skin-temperature readings, there was noted marked increase in the sweating of the hands and feet and also such severe axillary sweating as to cause the patient embarrassment. After procaine nerve block, there was a prompt and spectacular decrease in the moistness of the treated foot.

Amaurosis fugax

Under this heading may be considered all those ocular disturbances that are transitory in nature, borderline in character, and that produce certain symptoms and signs due to autonomic instability, but leave no permanent, visible, organic change. These conditions may be listed as: (1) transitory visual loss under conditions of emotional stress; (2) visual disturbances under conditions of extreme fatigue, such as that seen in combat fatigue in the armed service.

Under the first of these headings may be placed the very numerous cases seen in young adolescents of somewhat unstable temperament, who manifest periodic "black out" under conditions of excitement, homesickness, worry, and the emotional shock of battle. Every medical officer in the Armed Forces has seen them in great numbers, and I have frequently seen them in civilian life in anxious medical students before or during an important examination. Within the past six months, I have so often encountered this symptom in patients with typical neurocirculatory asthenia as to consider it of considerable importance as a diagnostic sign of that "disease." The patient is rarely sick enough to be hospitalized but is seen in consultation in the out-patient clinic. His chief complaint is of frequent, periodic loss of vision in both eyes lasting upward of 30 seconds. The visual loss is described as a "fogging" of varying degree, sometimes culminating in complete "black out" as described by aviators at the termination of a dive, when the sudden change of direction of the plane forces the pilot downward so hard as to drain the blood from his cerebral vascular system (and possibly from the retina) into the extremities and splanchnic reservoirs. One outstanding case of this sort occurred in a fighter-plane pilot, who compared his periodic visual loss with that occurring in the "pull out" from a plane dive.

In all of these cases, there is definite, clinical evidence of hyperactivity of the sympathetic nervous system. Many of them show evidence of some degree of vasospasm, so that the tips of the fingers are cold and sometimes cyanotic. The most frequent and annoying associated symptom, however, is hyperhidrosis. These patients almost uniformly show a clammy wetness of the hands and feet which, under the mild psychic stress of questioning and examinations, becomes so marked that their hands drip beads of perspiration and everything they touch becomes wet. Also frequently noticed is a remarkable degree of axillary sweating, so that after a few minutes of questioning the patient is much embarrassed by large stains which appear on his shirt sleeves. There is no increase in generalized sweating, and comparisons of the patient's hands with those of medical corpsmen in the same room reveals a marked difference.

Careful ocular examination of these cases, including exhaustive muscle-balance tests, cycloplegic refraction, ophthalmoscopic examination, and visual-field tests revealed no objective findings of note.

Six men suffering from "combat fatigue" who complained of visual disturbance, have been seen in consultation with the neuropsychiatric departments. Of these, only one showed demonstrable organic change in the retina and some permanent visual disturbance. All six showed classical symptoms and history of combat fatigue, with the additional rather unusual history of frequent, transitory, visual loss lasting from a few seconds to over a minute.

TABLE 4

CENTRAL ANGIOSPASTIC RETINOPATHY—TREATMENT

Case	Intravenous Typhoid dose in millions	Sodium Nitrite daily dose	Nicotinic Acid daily dose	Aminophyllin daily dose	Case	Intravenous Typhoid dose in millions	Sodium Nitrite daily dose	Nicotinic Acid daily dose	Aminophyllin daily dose
		mg.	mg.	gr.			mg.	mg.	gr.
1	5, 10, 25	100	—	—	21	10, 25, 25	100	—	—
2	5, 10, 25	100	—	—	22	10	100	150	7.5
3	—	100	—	—	23	5, 10, 25, 25	100	150	7.5
4	10, 20	—	—	—	24	—	—	—	—
5	—	—	—	—	25	10, 10	—	150	7.5
6	5, 10, 25, 25	100	100	7.5	26	—	—	150	7.5
7	—	—	—	—	27	25	—	150	7.5
8	—	100	—	—	28	—	—	—	—
9	—	—	—	—	29	10, 25	—	150	7.5
10	—	—	—	—	30	—	—	—	—
11	—	—	—	—	31	5, 10, 25, 25	—	150	7.5
12	10, 25	100	—	—	32	5, 10, 10, 10	—	150	—
13	—	—	—	—	33	5, 10, 10, 10	—	150	—
14	10, 25	100	—	—	34	—	—	—	—
15	—	—	—	—	35	5, 10, 10, 10	—	150	7.5
16	—	—	—	—	36	10, 10, 25	—	150	7.5
17	—	100	—	—	37	10, 15, 25	—	—	—
18	5, 10, 25	100	100	7.5	38	10, 15, 25	—	—	—
19	10	100	—	—	39	5, 10, 15, 25	—	150	7.5
20	—	—	—	—	40	—	—	—	—

CASE REPORT

W. H., seaman first class, aged 25 years, was admitted to the hospital on the neuropsychiatric service with the diagnosis of combat fatigue. He had been stationed aboard a ship which had participated in four major sea battles and which had been twice struck by bombs and once by shell fire from an enemy cruiser. He had never been particularly nervous in temperament, had a very stable background, and a good family history. He admitted that he frequently had been frightened and tense, and stated that this fear had increased in severity to such a degree that in the last few months of service every call to general quarters found him hyper-alert and trembling. Because of this nervousness, he had increased his cigarette consumption from 15 to 80 cigarettes a day. He first noted a blurring of vision following a night battle. After the action had broken off and the "secure" signal was given, he returned to his quarters to find that objects were blurred and "misty." In about a minute, vision cleared. He attributed this phenomenon to exposure to gun flashes near by and to his staring into the dark for so long. Shortly after this, he began to experience rather frequent attacks of blurred vision which seemed to occur when he was tired or excited. He states that these attacks were not associated with reading or other use of his eyes. Two weeks before entry to the hospital, his ship was struck by an enemy bomb.

The explosion was at some distance from him and although he was knocked up against the bulkhead, he was not dazed or otherwise hurt, except that he felt like he was "going all to pieces." He began to tremble violently and completely lost his vision. He was found by a medical corpsman groping about the deck on his hands and knees and crying, and was taken to the sick bay. His vision gradually returned, and he believes that the total elapsed time of the visual loss was not more than 15 minutes. Since that time, however, he felt that his vision was not so good as before.

On admission to the hospital, he was found to be very nervous and apprehensive, with definite tremor of the hands and marked sweating of the palms. He frequently experienced severe nightmares from which he awoke crying. The least noise elicited a severe "startle reaction."

Examination of the eyes showed vision to be: R.E., 20/40; L.E., 20/25. Refraction with cycloplegic showed, R.E., a + 0.50D. cyl. ax. 90°; L.E. +0.25D. sph. Vision was not improved by correction of this error. The macula of the right eye showed the typical granular pigmentation with loss of the foveal reflex seen in central-angiospasm retinopathy. The macula of the left eye was normal in appearance.

It was felt that this case might well be placed in the classification of angiospastic retinopathy, except that the organic findings were so minimal and the visual loss was of a transitory character until the final attack.

Under rest and sedation and a minimum of psychotherapy, the patient's general symptoms cleared rapidly.

Of retinal angiospasm in general, Duke-Elder[20] points out that its recognition as a cause of amaurosis fugax is of relatively recent date. It can be produced experimentally by injection of adrenalin or of the serum of hypertensive individuals, or, in susceptible persons, by cold, or by the inhalation of tobacco smoke. The actual observation of spasmodic contractions of the retinal vessels, of fleeting duration, associated with similar vascular phenomena elsewhere and leaving no trace, has established the condition as a clinical entity.

Cases of retinal angiospasm occurring in young individuals who show no signs of organic retinal arterial diseases are frequently associated with evidence of vasomotor instability elsewhere.

Migraine

Although typical ophthalmic migraine is a cerebral rather than an ocular disturbance, it can scarcely be doubted that it is of vasomotor origin. As its chief manifestations are ophthalmic, it is included here.

The incidence of typical ophthalmic migraine (with homonymous scintillating scotomas and transient homonymous hemianopia, followed by headache, nausea, vomiting, and prolonged lassitude) is extremely high in the armed services.

This may be because we are dealing almost exclusively with the age group commonly subject to the disorder. It has been my experience, however, that careful questioning of many individuals reveals a definite background of long-standing, mild vasomotor instability that has been markedly aggravated by psychic trauma incident to duties in the Service.

A typical case will frequently include a family history of migrainous attacks in the mother, or sibling, or both. The past history reveals infrequent, but typical, migrainous attacks beginning as early as 8 to 10 years of age. Cautious questions will elicit the information that these attacks were usually precipitated by an unpleasant experience or in anticipation of some disagreeable situation. On entering

the Service, the attacks usually increase in frequency and severity during early adjustment in boot camp and then subside somewhat, only to break out anew with a change of duty—particularly in anticipation of foreign duty. In at least two instances in officer personnel, a series of violent and completely disabling attacks were precipitated by assignments to new commands entailing greatly increased responsibility. In three cases, I have precipitated attacks, in which I was able to map out congruous homonymous hemianopias, by announcing to the patients that I was discharging them from the hospital back to full-duty status.

A large percentage of the cases of typical ophthalmic migraine which I have examined have shown clinical evidence of generalized vasomotor instability, as judged by the critera set forth, especially hyperhidrosis.

In only one case was I able to demonstrate an actual spasm of a retinal vessel during the prodromal attack of scintillating scotoma, although this has been frequently described in the literature. In no case have any permanent organic ocular or cerebral changes been noted.

It is recognized that cognizance must be taken of the other theories of the etiology of migraine, such as precipitation of attacks by food allergy, but in the vast majority of the cases examined by me, the etiologic factor was almost undoubtedly vasomotor, and the usual precipitating factor was psychic trauma.

Commotio retinae

Under this classification will be considered the retinal changes incident to localized vasospasm resulting from: (1) ocular contusion; (2) blast concussion; (3) solar burns.

In a recent letter to the Navy Department, Bureau of Medicine and Surgery News Letter, Prof. Alton Ochsner[28] stated:

> As a result of trauma, vasoconstriction of peripheral arteries invariably occurs. This is undoubtedly a protective mechanism and is lifesaving at times. The trauma initiating the vasospasm can be of any type: mechanical, accidental, operative, thermal or actinic. The greatest degree of vasospasm is seen apparently in crushing injuries and in frost bite.
>
> The degree of vasospasm varies considerably in different individuals. Under some conditions and in some individuals, the degree of vasospasm may be so slight as to produce few, if any, manifestations. On the other hand, it may be so severe as to produce such ischemia that gangrene may develop. This condition has been designated as "local shock."
>
> In addition to the actual necrosis and interference with wound healing which may result from the vasospasm associated with trauma, there may occur interferences with sensations, particularly sympathalgia, the so-called causalgia which previously has been difficult to explain. Many individuals with this condition were considered as malingerers, since the location of their pain did not correspond to the distribution of the peripheral nerves.

With vasoconstriction due to mechanical, thermal, or actinic trauma, there is a secondary dilatation of the minute vessels in the area, as previously stated in the discussion of chemical control of the circulation.

As has been pointed out, substances of the nature of histamine are produced locally by the tissue cells as the direct result of any trauma sufficient to liberate histamine from the cells. The complete reaction produced by these histaminelike substances is a primary and local dilatation of the minute vessels, a local increase in the permeability of the capillary walls, and a widespread dilatation of neighboring arterioles.

The reactive hyperemia that occurs after obstruction of the circulation is an example of this dilatory action of local-tissue metabolites. Heat, light, or ultraviolet radiation dilates the capillaries through the same mechanism of histamine liberation.

In considering commotio retinae, under which we have classified the retinal changes associated with ocular contusion, blast compression or concussion, and solar retinitis, we are dealing with morphologic changes in the macula which are practically identical in each case.

Duke-Elder[20] has pointed out that one of the sites of election for retinal edema is the macula. In states of circulatory edema, this is probably due largely to the structure of the thick fiber-layers of Henle, which absorb large quantities of fluid, and to the avascularity of the central area. Such edema follows contusions to the globe and probably depends, as in the brain, upon a sudden vasoconstriction followed by an extreme vasodilation.

In commotio retinae from whatever cause (contusion, concussion, or thermal), the ophthalmoscopic picture is practically identical, varying only in degree. It is so remarkably similar to the clinical picture seen in central angiospastic retinopathy and also in the two cases of Raynaud's disease previously described as to defy ophthalmoscopic differentiation.

In its milder aspects, the edema produced is sometimes difficult to see. The retina in the macular area looks thicker and somewhat translucent; with a finely granular appearance and a series of radiating, somewhat spokelike reflexes. Occasionally, the entire macula will be surrounded by a bright "halo reflex," such as has been described in connection with angiospastic retinopathy.

This edema may persist for days to weeks but gradually subsides, leaving in its wake a definite and sometimes marked redistribution of pigment. In many instances, this is imperceptibly followed by autolysis of the retina in the foveal area, with production of the typical "hole" in the macula.

The only difference between this picture and the classical Berlin's opacity, with its milky clouding of the retina, is one of degree.

It was a striking clinical feature of all three types of commotio retinae that the majority of the patients complained rather bitterly of a nagging, boring type of orbital pain which was very persistent and similar in every respect to the pain noted so frequently in the angiospastic cases. It is thought that this is probably a form of causalgia or sympathalgia.

Contusion retinopathy

Case 1. L. W., aged 22 years, was struck in the right eye by a hand ball. There was immediate and marked loss of vision and pain in the eye, Examination that same afternoon showed an injected eye with traumatic dilatation of the pupil, edema of the lid, free cells in the aqueous, but no hemorrhage. Vision was finger counting at two feet. The macula of the right eye showed the grayish, translucent appearance of a moderately severe Berlin's opacity, with elevation of the retina in the macular area. During the next few days, the vision improved rapidly and the retinal edema subsided. The patient complained of severe pain deep in the orbit "behind the eye." As vision improved, the tangent-screen field showed a small central scotoma for the 2/2,000 isopter.

At the end of a week, vision was 20/70 in the right eye, and the retina had regained its normal transparency, although it still showed some edema and a definite granular pigmentation of the macula. The foveal reflex was absent.

Two months later, reëxamination showed a typical small "punched-out hole" in the macula, and vision was 20/30. The pain in the orbit was still present, although decreasing in severity. A minute central scotoma was still demonstrable, and there was definite metamorphopsia, as tested by the "music-staff" test at 14 inches.

Case 2. C. B. P., a 20-year-old corporal of Marines, was injured on Iwo Jima. A bullet went through the right maxilla from below the right ear and "exploded" in his mouth. A large hole was torn in the palate and into the right antrum. There was moderate exophthalmos of the right eye. On examination, 10 days after injury, vision of the right eye was 20/30. The macula showed definite and fairly marked edema with granular pigmentation around the fovea and striate folding of the retina around the fovea. Reëxamination, three weeks later, showed subsidence of most of the retinal edema but with marked increase in foveal pigmentation and no improvement in corrected vision. No scotoma could be demonstrated, but metamorphopsia was fairly marked.

Case 3. H. E. E., a 21-year-old private of Marines, was pushing a 37 mm. gun over rough terrain on Iwo Jima when the gun ran over a land mine. The gun was blown to bits. The patient was behind the steel shield and sustained some shrapnel wounds in his legs and lower trunk, and a few in his arms and face. He was unconscious for two days. When he regained consciousness, he could not see from either eye for another two days. Then vision in the right eye gradually returned. He believes he was struck in the face by a piece of the gun as the lids of both eyes and his nose were severely swollen and bruised.

Examination, 16 days after the injury, showed vision to be R.E., 20/40; L.E., light perception. The left eye showed a dislocation of the lens medially through rupture of the lateral zonule. The macula of this eye showed a very marked gray edema, with a dark-red spot in the fovea. Next to the disc was a small streak of traumatic choroiditis, or rupture of the choroid.

The right eye showed a coarse, granular pigmentation with a faint halo around the macula, as seen in minor degrees of edema. There was a very small scotoma for a 1-mm. object at 1 M., just at the upper edge of fixation. The clinical picture was identical with that seen in a subsiding angiospastic retinopathy. The patient had many of the signs and symptoms of combat fatigue, such as, startle reaction, tremor, nightmares, and anxiety. He also showed marked sweating of the hands and some coolness of the fingers. It was considered that the left eye showed definite evidence of contusion, with secondary angiospastic retinopathy. The findings in the right eye could be due to minor contusion, blast compression, or even severe psychic trauma. They serve to demonstrate the similarity in all three forms regardless of the etiology.

Blast concussion

Case 1. H. L. M., a Marine Corps second lieutenant, aged 26 years, was injured by the blast from an exploding ammunition dump which went off about 100 yds. from him. He thought that seven or eight men near him were immediately killed by the blast. At the moment of the explosion, he was in a foxhole leaning down in an attempt to help his commanding officer, who had been injured by shell fire. Although he was blown from the hole, he was not struck by shell fragments and felt that the force of the blast was broken, thus saving his life. He was unconscious for six days and suffered some bleeding from ears and nose. Both ear drums were ruptured, but quickly healed. When he regained consciousness, he was almost completely deaf, and vision was little more than good light perception. Both hearing and vision rapidly improved, and in five days, vision was recorded as: R.E., 20/30; L.E., 20/40. On examination, three weeks after injury,

vision was: R.E., 20/25; L.E., 20/30; corrected to 20/25 (blurred) in each eye with a −0.50D. cyl. ax. 90°. He had previously always had 20/20 vision, uncorrected, in each eye. Hearing was decreased in the right ear, 20 percent; in the left ear, 50 percent.

Both maculas showed granular pigmentation with some residual edema. The fovea of the left eye showed a minute, sharply outlined, red spot which looked like a small crater. No scotoma was demonstrated but metamorphopsia could easily be elicited in the left eye. The patient had shown some signs of combat fatigue including a severe tremor and very marked hyperhidrosis, but these had practically disappeared after three weeks, and he was anxious to return to duty.

Case 2. V. J. P., a 22-year-old seaman, first class, was blown 10 ft. or more across the deck of his ship by the explosion of a Japanese suicide dive bomber, containing a warhead which struck the ship. He thinks he was about 30 ft. from the plane when it struck. He was unconscious for several minutes, and there were several casualties near him. When he regained consciousness, he was blind but otherwise unhurt, except for some minor lacerations about the face and chest. He was dioriented, dazed, and almost completely blind for two days. Vision gradually improved in both eyes but remained blurred in the right eye. Examination, two weeks after the injury, showed vision to be: R.E., 20/40; L.E., 20/20. External examination of both eyes and X-ray pictures of both orbits were negative. Pupils were normal and media clear. The fundus of the left eye was normal; that of the right eye showed a grayish, translucent edema of the entire macula, with a small reddish spot in the center. Tangent-screen field showed a 2° central scotoma for the 1/2,000 isopter. Reëxamination in two weeks showed the retinal edema to have partially subsided but to be still easily visible, with considerable increase in foveal pigmentation and the appearance of an early hole in the macula. There was no evidence or history of contusion of the eye by a solid object.

Solar retinitis

Only two cases have been seen which I felt could be unquestionably called solar retinitis. Many cases of macular pigmentation, macular edema, and hole in the macula have been reported from the Pacific area of war and have been attributed to damage by actinic rays because of their history of exposure to glare from coral sand and water. Thygeson[29] reports seeing many such cases in aviators after repeated high-altitude flights. It is possible that some of these cases were actually due to the action of infrared or ultraviolet rays on a sensitive retina. Their description, however, tallies much more nearly, both as to subjective symptoms and objective signs, with angiospastic retinopathy produced by vasomotor disturbances initiated by psychic trauma, fatigue, or increased use of tobacco in an autonomically unstable individual.

I have seen some of these cases returned to the United States from the Southwest Pacific with the diagnosis of actinic-ray ophthalmia and have compared them with severe cases of central angiospastic retinopathy from the Aleutian Islands area where exposure to the sun was not an etiologic factor. In their end stages, they are clinically identical.

Some years ago Verhoeff and Bell[30] exposed an eye that was to be enucleated to prolonged ultraviolet irradiation with resulting loss of vision but with very rapid recovery. They were unable to demonstrate any retinal lesions due to ultraviolet rays.

The same authors showed that the

effects known as "eclipse burn of the retina" were wholly thermic and due to concentration of solar energy upon the retina by the refractive system of the eye itself. Although there have been undoubted examples of eclipse blindness, the majority of such cases give but a vague and indefinite history of exposure and visual loss.

In the two cases of solar retinitis to be reported, there was unquestioned exposure to direct sun rays, augmented by concentration of the rays by optical instruments.

Cordes,[19] in his report for the National Research Council, cites several practically identical cases described to him by various Naval medical officers.

Case 1. W. H., a 26-year-old seaman, first class, was stationed as lookout on a small aircraft carrier. He was using a monocular telescope and searching for enemy planes. Since, in attacking, the planes usually "come in from the sun," he had kept his glass focused in that general direction and had noticed several transient blurrings of vision which, however, rapidly cleared. Upon receiving a report that planes were approaching, he had looked directly into the sun and immediately noticed a very sharp and severe pain in the eye and a complete obscuration of vision. The pain continued to be very intense and seemed to be located deep in the eye or orbit. Vision was limited to light perception. Upon examination in the sick bay, a note of "a marked haziness of all the retina temporal to the disc" was made in his health record. When hospitalized one month later, vision in the right eye was reduced to 20/200. There was still some edema of the macula of the right eye and considerable pigment disturbance; the fovea was replaced by a deep-red, "punched-out" hole. The pain in the eye was still severe.

Case 2. P. J. T., a boatswain's mate, second class, aged 29 years, was acting as lookout aboard his ship and inadvertently followed a plane directly "into the sun" with a pair of binoculars. There was immediate severe pain in both eyes and marked loss of vision so that he had to be led into sick bay, where examination showed a "grayness of both retinas temporal to the disc, with a small hemorrhage in its center." It is thought that this "hemorrhage" was the red spot in the fovea which, when seen three days later, showed the typical picture of bilateral Berlin's opacity of the macula.

Vision was reduced to 4/200 in each eye, upon examination in the hospital. There was gradual improvement in vision during the next month and when last seen, vision was: R.E., 20/70; L.E., 20/100. There was a heavy granular pigmentation of both maculas, with sharply outlined holes developing in both foveae.

These lesions are thought to be the result of localized vasospasm of the retinal arterioles and capillaries in the macula initiated by thermal or infrared rays and followed by compensatory vasodilation, increased capillary permeability, severe edema, autolysis of the retina, and, finally, hole in the macula.

Summary and Conclusions

1. The relationships between the eye and the autonomic nervous system are reviewed with special reference to possible effects on ocular physiology.

2. The autonomic stimuli are enumerated and found to be intensely active under wartime condtions of living. Special emphasis is placed on the importance and frequency of psychic trauma as a cause of autonomic instability and of the production of both physiologic or functional and pathologic or organic ocular changes.

3. Clinical studies have been made on autonomically unstable individuals, including certain studies on the peripheral vascular system. These have been correlated with certain physiologic dysfunctions and pathologic changes in the retina.

4. The clinical picture of vasoneurotic diathesis of the autonomically unstable person is described, and it is noted that the only constant factor in all cases of central angiospastic retinopathy is this autonomic instability.

5. The ocular manifestations of autonomic-nervous-system dysfunction reported were as follows: (a) central angiospastic retinopathy; (b) ocular changes in Raynaud's disease; (c) amaurosis fugax; (d) migraine; (e) commotio retinae. Typical case reports of each condition are presented.

6. It is emphasized that the differences between amaurosis fugax, central angiospastic retinopathy, and Raynaud's disease are those of degree only.

7. The condition known as Migraine is a cerebral vasospastic disturbance with predominant ocular symptoms.

8. Commotio retinae, which embraces all conditions producing retinal edema from chemical vasomotor disturbances, is a local rather than a general autonomic response.

9. Psychic trauma in a susceptible individual can produce as profound organic changes in connection with the autonomic nervous system as extremes of temperature, anoxemia, or direct physical trauma. The greatly increased wartime incidence of certain disturbances of autonomic origin can be explained in no other way.

10. The almost constant association of pain with these ocular lesions can best be explained as causalgia or sympathalgia.

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PEMPHIGUS CONJUNCTIVAE*

Report of three cases

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Pemphigus conjunctivae is a slowly progressive, chronic, cicatrizing, keratoconjunctivitis of unknown etiology, frequently associated with vesicular lesions of the mucous membranes and occasionally with cutaneous involvement. It is characterized by an absence of constitutional symptoms and a benign course as concerns life.

Pemphigus is usually classified as acute and chronic pemphigus vulgaris, pemphigus vegetans, pemphigus foliaceus, pemphigus erythematosus (Senear-Usher), and pemphigus conjunctivae or benign mucous-membrane pemphigus. The latter type has been described as a distinct entity by Klauder and Cowan,[1] who distinguish it from chronic conjunctival shrinkage and scarring accompanying a number of skin diseases, most of which exhibit blebs (bullous eruption following vaccination, dermatitis herpetiformis, erythrodermia ichthyosiformie, and epidermolysis bullosa dystrophica). The condition known as acute ocular pemphigus and characterized by a pseudomembranous conjunctivitis, stomatitis, severe prostration, and a cutaneous eruption is classified by them as a severe atypical form of erythema exudativum multiforme (Hebra).

The incidence of pemphigus conjunctivae is probably greater than previously believed. Lever and Talbott[2] saw 62 cases of pemphigus at Massachusetts General Hospital between 1921 and 1936, 10 of which (16 percent) were of the conjunctival type. Rycroft[3] saw four cases at Moorfield's in five years and believed the disease was not uncommon. Cutaneous pemphigus, particularly pemphigus vulgaris, is more common and is associated with a higher mortality in Jews, but no racial difference has been noted in the conjunctival type. There is a relatively even distribution between sexes in the cutaneous types, but the conjunctival form occurs more commonly in the female. The disease is usually one of later life, the average age in Lever and Talbott's[2] series of 10 cases being 61.6 years.

Parsons[4] states that early in the disease the conjunctiva shows considerable swelling due to edema and lymphoid infiltration. Later, the conjunctival epithelium is much thickened and sends coarse plugs into the subconjunctival tissue. There is marked infiltration of the submucosa with round and spindle cells and enormous hypertrophy of fibrous tissue.

Lever and Talbott[5] found a reduction in blood-serum protein, sodium, calcium, and chlorides in acute and chronic pemphigus vulgaris and pemphigus vegetans but no serum abnormalities in the conjunctival type. Mulvehill[6] found consistently low serum albumin fractions in 10 cases of pemphigus but in no case was there ocular involvement. Pels and Macht[7] have devised a test which depends upon marked inhibition of growth of *Lupinus albus* seedlings when immersed in a nutrient solution containing pemphigus blood serum. It has been positive in all types of pemphigus including pemphigus conjunctivae.

There are no symptoms characteristic of the ocular phase of the disease. Ini-

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tially, patients complain of a moderate photophobia, burning, itching, and similar complaints associated with a mild, chronic conjunctivitis. In the later stages, intermittent conjunctival injection, dryness, and persistent foamy, ropy secretion are most prominent. Formation of symblepharon and conjunctival scarring develops insidiously and without a readily apparent ocular inflammation. Cicatricial contracture may cause trichiasis, and the symblepharon may become so extensive as to cause complete ankyloblepharon with ultimate loss of the globe. The cornea may be covered with a cuticularlike membrane with serious diminution of vision long before involvement secondary to complete ankyloblepharon.

The mucous membranes of the nasal pharynx, mouth, esophagus, rectum, and vagina are frequently involved. Early, there are vesicles of varying size which eventually rupture, leaving macerated areas. These areas heal slowly and result in atrophic scarring and contracture with deformity in the part involved.

The skin is infrequently involved according to most writers. However, Urbach[8] states that pemphigus of mucous membranes may exist for one, two, or three years, and then suddenly break out over the entire body. The skin eruption is usually localized particularly on the face and initially presents blebs which rupture and then crust. The lesions heal slowly without scarring. The presence of cicatricial changes in the skin has been described rarely, Lever[9] finding but five cases previously reported to which he added six of his own.

Numerous theories as to the cause of pemphigus have been proposed but none confirmed. Among these theories are the toxic, neurotropic, infectious (B. pyocyaneus, B. pemphigus, B. streptococcus), vitamin deficiency, virus (Urbach), and suprarenal insufficiency. Recently Gallardo and Hardy[10] isolated a virus closely related to the vaccinia virus in a case of pemphiguslike keratoconjunctivitis.

The status of treatment of pemphigus has not changed since 1930, when Riecke[11] wrote: "Pemphigus shows such a fitful and paradoxic spontaneous course that only too easily can erroneous conclusions on the value or lack of value of any line of treatment be drawn." This statement is emphasized by the number of drugs which have been recommended and condemned. In the text by Ormsby and Montgomery,[12] the following treatments are mentioned: quinine, arsenic as sodium arsenate, acetarsone (stovarsol), salversan, cacodylate of iron, tryparsamide, soluble mercurochrome, moccasin venom, germanin, exclusion of salt from diet, colonic irrigations, strychnine, autogenous vaccine, cod-liver-oil and malt preparations, viosterol, and sulfanilamide. Recently, in a careful study, Lever and Talbott[5] have used adrenal-cortical extract and dyhydrotachysterol with encouraging results in all except pemphigus conjunctivae, in which the course of the disease in two patients was not affected.

Trichiasis and xerosis are frequent ocular complications. Dimitry[13] recently recommended the use of choline as a wetting agent in ocular pemphigus and stated that the local use of the drug has made epilation unnecessary. The Van Milligan operation is of transient value only, as the transplanted mucous membrane is eventually converted to scar tissue together with the adjacent conjunctiva. Surgical separation of the symblepharon is of no value, for the adhesions re-form, in spite of any agent placed between the epithelial surfaces.

Case reports

Case 1. A 26-year-old, white soldier, was admitted to Wakeman General Hospital, November 19, 1945, complaining of

recurrent redness of the eyes. He stated that, while hospitalized for pneumonia in November, 1944, he had developed a mucopurulent conjunctivitis which had recurred intermittently ever since. In July, 1945, a severe skin inflammation, diagnosed as impetiginous dermatitis, cleared with penicillin systemically, but since then had recurred about the face every few weeks. When 4 years old, he had a severe dermatitis with sores over the body and, when aged 9 years, had an empyema which necessitated a rib resection. He gave a history of high fever and general prostration whenever he received sulfonamide drugs.

Uncorrected vision in each eye was 20/20. The conjunctiva was atrophic and deeply scarred, particularly over the tarsi. A ropy, white secretion was present in the inferior fornices. The cul-de-sacs were markedly shortened and contained linear, horizontal, white scars which were elevated above the adjacent conjunctiva. Symblepharon bound the atrophic caruncles to the lower lids, and the semilunar folds were obliterated by adhesions between their free edges and the globe. A symblepharon extended from the inner margin of the upper lid to the globe, and traction of the lid resulted in an ischemic linear area extending from the point of adhesion to the corneal limbus.

Physical examination showed bilateral, chronic, maxillary sinusitis and right basilar bronchiectasis, which were asymptomatic.

Blood-serum protein, chlorides, calcium, cholesterol, nonprotein nitrogen, sugar, and sedimentation rate were normal. Agglutination for brucella and tularemia were negative as were the Kahn, Frei, and Mantoux tests. The white blood count was within normal limits, and the differential showed no abnormality other than an eosinophile count of 4 to 6 percent.

A small section of the right, lower lid was normal except for moderate round-cell infiltration of the subepithelial tissue.

At no time were vesicles of the conjunctiva, mouth, or pharynx noted and, other than the conjunctiva, there was no mucous-membrane involvement. Crusting lesions of the face were present intermittently and responded quickly to penicillin intramuscularly. Penicillin (1,000 units to 1 c.c. in solution) used locally in the eyes caused much of the secretion to disappear and seemed to limit the number of attacks of the conjunctival inflammation, but the condition remained essentially unchanged during four months of hospitalization.

Case 2. A 28-year-old, white soldier was admitted to Wakeman General Hospital, January 15, 1946, complaining of dryness and recurrent inflammation of the eyes present since March, 1942. He had been hospitalized at that time for pneumonia and treated with a sulfonamide drug to which he was sentitive. A concomitant conjunctival infection was treated with sulfathiazole ointment and caused a severe local reaction. Since then, the ocular inflammation had recurred periodically but was not incapacitating.

Vision was 20/70 in each eye corrected to 20/30 with a -1.25D. sph. $\bigcirc$ $+3.50$D. cyl. ax. 90° in the right eye; and a -1.00D. sph. $\bigcirc$ $+3.00$D. cyl. ax. 95° in the left. The palpebral conjunctiva showed diffuse atrophic scarring and several symblepharon extended from the inner margin of the upper lid to the globe. The semilunar folds were obliterated by adhesions, but the caruncles showed no scarring. In the outer portion of each inferior cul-de-sac, the conjunctiva was thrown into folds and appeared redundant but was firmly adherent to the underlying tissue. The remainder of the ocular examination was negative.

The hard palate showed white scars extending from the teeth to the median raphe, and, on one occasion, a macerated, red area was present on the buccal mucosa of the cheek. Vesicles formed occasionally on the gums and ruptured but did not appear to cause scarring. A vertical, linear scar was present on the left inferior turbinate. The remainder of the physical examination was negative.

Blood-serum protein, chlorides, calcium, cholesterol, sugar, and sedimentation rate were within normal limits. The Kahn, Frei, and Mantoux tests were negative, as were agglutination for brucella and tularemia. The white blood count was normal and showed 2-percent eosinophiles. A small section of tissue removed from the left, lower eyelid revealed no pathologic changes.

The patient's condition remained unchanged during hospitalization. Vesicles of the gum and mild, recurrent conjunctival injection were the only evidence of activity. The skin was not involved at any time.

Case 3. A 23-year-old, white soldier was admitted to Wakeman General Hospital, from overseas, May 30, 1945, complaining of diminution of vision and marked weakness. He had been wounded in the right foot and taken prisoner in Germany, November 15, 1944. While hospitalized for the foot wound, he developed a severe dermatitis of the head and neck which caused his eyelids to swell to complete closure. He was treated at an eye clinic, and the inflammation subsided, but vision was severely impaired. After recapture in April, 1945, the diagnosis of pemphigus conjunctivae was suggested by H. A. Mosher, Capt. (MC), at an Army General Hospital in Europe. In the course of evacuation to the United States, the patient developed a weakness of the lower extremities and was unable to walk.

He stated that impetigo had covered his body in 1943 and had disappeared without residue. Other than this, his medical history prior to capture was essentially negative.

Vision was: R.E. 20/300, corrected to 20/40 with a +3.75D. sph. ⌒ −7.00D. cyl. ax. 40°; L.E., 20/400, corrected to

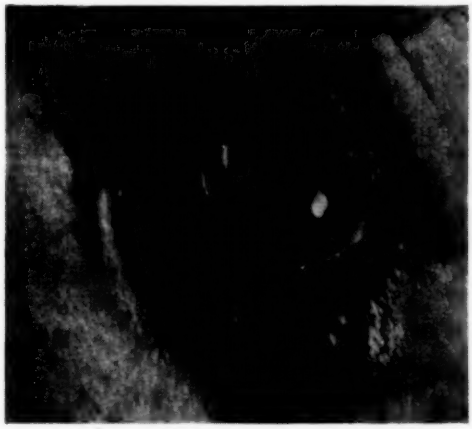

Fig. 1 (Newell and Greetham). Case 3. Symblepharon involving cornea.

20/50 with a −1.25D. sph. ⌒ −1.75D. cyl. ax. 45°. The conjunctiva was shrunken, diffusely cicatrized, and pale in appearance, with many blood vessels obliterated by scar tissue. The cul-de-sacs were shallow, the caruncles scarred with numerous discrete linear areas, and the semilunar folds obliterated. A large number of symblepharon were present in the superior fornices, which were adherent to the globe. The left eye showed a heavy symblepharon which swept down from the superior lid margin to the inner one half of the cornea. A diffuse opacity, deep in the substantia propria, was present immediately temporal to the attachment of the symblepharon to the cornea. A large number of superficial epithelial opacities were present bilaterally. The circumference of the limbus showed diffuse clouding of the substantia propria extending inward 2 to 4 mm. and covered

with superficial, new blood vessels which, in some areas, extended beyond the opacity. The irides were slightly atrophic and bound to the anterior lens capsule by numerous darkly pigmented synechiae. The anterior capsule of each lens was diffusely opaque, particularly the left. There was no aqueous flare, and the remainder of the ocular examination was negative.

Physical examination revealed a healed bullet wound of the right foot, generalized muscle tenderness, absence of the cremasteric and patellar reflexes, and a hypoesthesia to the level of the second lumbar segment. The skin of the posterior surface of the right calf and anterior surface of the left wrist showed circular, atrophic scars, measuring 2 cm. in diameter, depigmented centrally, with a ring of pigment at the periphery.

Blood-serum protein, chlorides, calcium, cholesterol, nonprotein nitrogen, and sedimentation rate were normal. The albumin-globulin ratio was reversed on several occasions. Agglutination for brucella and tularemia were negative as were the Frei, Kahn, and Mantoux tests. White blood count was normal, but the differential showed 5-percent eosinophiles.

The patient was placed on a high caloric, high nitrogen, and high fat diet, supplemented by vitamins orally and parenterally, and given 300,000 units of penicillin intramuscularly in divided doses. In several weeks, the muscle tenderness and hypoesthesia disappeared, and the deep-tendon reflexes returned. Locally, atropine, adrenalin, cocaine, and neosynephrine were used in an attempt to break the posterior synechiae, and penicillin was used as an antiseptic. The cataract in the left eye progressed to maturity and vision diminished to light perception. On several occasions, multiloculated vesicles were noted at the corneal limbus of the right eye and on the conjunctival surface of the lower lids. They did not rupture on repeated examination and disappeared spontaneously after four or five days. They were not associated with gross inflammation of the eye and did not give rise to symptoms. There has been no increase in the number of symblepharon since admission to this Hospital, and the lens opacity in the right eye has remained stationary.

Comment

A number of eye and skin diseases associated with conjunctival scarring and shrinkage were considered in making the diagnosis of pemphigus conjunctivae in these patients. There was no history of ocular injury with chemical agents, and the onset of the disease was not associated with vaccination. Trachoma was excluded in the absence of corneal involvement with typical pannus formation, lack of papillary hyperplasia, and the large amount of symblepharon formation. Erythrodermia ichthyosiformie and epidermolysis bullosa dystrophica are largely congenital conditions and have their onset in infancy. The absence of pruritic skin lesions, lack of involvement of the skin of the sacral triangle and scapular area ruled out dermatitis herpetiformis. The iodine-patch test was also negative in each of these patients and, while not absolutely diagnostic, indicated the disease was not dermatitis herpetiformis.

Grönblad[14] has described conjunctival shrinkage following sensitivity to luminal, and Kasselberg[15] has described a pemphiguslike skin eruption with symblepharon formation occurring in a patient sensitive to sulfamerazine. In that both Cases 1 and 2 gave a history of sensitivity to sulfonamides, it is possible that the ocular condition represented a drug sensitivity rather than pemphigus conjunctivae. The occurrence of vesicles in the mouth in Case 2 long after the drug was used led us to believe, however, that

the condition was not one of drug sensitivity. The large number of adhesions and the intermittent conjunctival injection continuing after the drug was discontinued indicated that the condition was most likely pemphigus conjunctivae in both cases.

The reversal of the blood-serum, albumin-globulin ratio observed in Case 3 was probably caused by nutritional deficiency rather than by pemphigus conjunctivae. The low degree of eosinophilia in each case is consistent with previous reports and is in contrast to the large increase in eosinophiles commonly seen in cutaneous pemphigus.

Bilateral uveitis with complicated cataract formation, as was present in Case 3, has not, to our knowledge, been reported previously as occurring in pemphigus. Although no etiologic factor was found, we believe that it occurred coincidentally rather than secondary to the pemphigus conjunctivae.

Penicillin was of no value in the treatment of the disease except that it appeared to lessen the amount of ocular secretion when used locally.

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THE EFFECTS OF ATABRINE ON THE HUMAN VISUAL SYSTEM*

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Atabrine (Quinacrine hydrochloride) is widely used today in the treatment of malaria. A review of the available literature fails to reveal reference to any temporary or permanent effects of this drug upon the human visual system. To this end, a study was undertaken to investigate (a) visual changes with increasing blood-atabrine levels, (b) any alteration with decreasing atabrine levels, and (c) the effects on vision of long-continued atabrine administration.

HISTORY

In the early campaigns in the Southwest Pacific area, malaria inflicted the greatest number of casualties, with a resultant serious impairment of the military effort. Quinine was limited and ineffectual. Atabrine was first used in widely varying dosages, and many side effects and clinical observations have already been recorded in the literature.

Most malaria was of the tertian form. There were many somatic complaints, including retrobulbar pains which were often aggravated by ocular effort. In many instances, these were definitely connected by the patient with a specific malarial recurrence. Refractive errors varied widely, and neuromuscular abnormalities were rarely seen. While perimetric examinations were invariably normal, a high rate of various-sized scotomas were found, seemingly proportional to the number of malarial recurrences. Finally, a group of our own medical officers returned from tropical service with some of the previously noted symptoms and changes.

Many other factors of possible etiology with unknown influence had to be considered: Retinal fatigue due to the tropical sunlight; cerebral fatigue and mental disturbances after combat; constitutional exhaustion following marked loss of weight common to combat; febrile tropical disease such as dysentery and dengue; and, lastly, the unknown toxic action of atabrine.

Solution of this problem was indicated, but the individual normal for each patient's system could not be determined in retrospect. Fortuitous circumstances permitted a scientific approach to the problem in that our organization, an affiliated general hospital, had been established for two years in an isolated subtropical section of Australia where the combat factors were absent and the use of any antimalarial drug had not been necessary. Furthermore, a change to tropical service was imminent. All of the illnesses and temperaments of the coöperating 39 officers with the requisite normal ocular systems and 6 others with minor small scotomas were well known. Because of these circumstances it was hoped to exclude all factors except those possibly connected with atabrine administration.

PART I: PROCEDURE

The basic preliminary examination of the visual tracts included the external inspection, the determination of visual acuities, neutralization of refractive errors with the aid of full homatropine cycloplegia, the detection of neuromuscular abnormalities, perimetric (1/2000/white and 3/330/white, blue and red/9 candlepower) and tangent screen (1/ and 6/2,000/white) investigations, and the actual sketching of the disc portion

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of the fundus. For the purposes of this investigation atabrine was issued in an experimental combination of dosages which individually were then officially recommended[2] in the Southwest Pacific area: 0.1 gm. daily, as in the suppression of clinical malaria (two weeks); 0.2 gms. daily, as in the rapid atabrinization obtained when approaching a hyperendemic area (one week); and in successive daily dosages of 1.2, 0.9, 0.3, 0.3, and 0.3 gm., as in full antimalarial atabrinization. Observations could thus be made at the different blood-atabrine levels. In actual clinical practice, a full course of atabrine for treatment would never be required immediately following 0.2 gm. per day for one week. The Chiefs of the Medical and Surgical Services selected eight of the volunteers to act as controls.

On the 7th, 14th, 21st, and 28th days, the basic examination was repeated except for the checking of the refractive errors. The laboratory determination of the blood-atabrine levels for the individual officers had to be discontinued because of technical difficulties. The theoretical group levels (based on the extensive studies at the Fort Knox Armored Research Laboratory, as reported in December, 1943)[1] were:

	Gamma per Liter
14 days at 0.1 gm.	16
additional	
7 days at 0.2 gm.	30
1 day at 1.2 gm.	67
1 day at 0.9 gm.	79
4 days at 0.3 gm.	73

Findings

Of the 45 officers who entered upon this part of the investigation, 6 controls and 32 taking atabrine completed it. The following data were recorded concerning of the 32 taking atabrine:

1. There were no changes in external appearance, in central visual acuity, in extent of fields with white or colored targets, or in neuromuscular action.

2. Tangent-screen examinations revealed that field changes appeared: (a) 17 officers developed 41 scotomas averaging 12.9 by 15.7 cm. in size. Twenty-four of these were within 20 degrees of the fixation point and varied in period of onset and in duration. (b) There was a gradual minor increase (to a total of 1 cm.) in the size of the blind spots, with increasing blood-atabrine levels. (c) The five initial scotmas showed decreased size in two cases, no change in one case, and increase with development of a second scotoma in two cases. (d) Ten officers had no demonstrable changes. (e) The changes may be tabulated as follows:

			16 gamma per liter calculated	30 gamma per liter calculated	79 gamma per liter calculated	
Start	1st week		2d week	3d week	4th week	5th week
Subjects	5	6	8	13	12	8
Scotomasa	7	9	15	19	26	11

3. Retinal changes found on ophthalmoscopic examination were limited to a slight increase in the pinkness of the discs. No capillary measurements were made.

4. Complications. Some of the clinical observations previously recorded by other authors[3] appeared in this study and are sufficiently pertinent to mention briefly: (a) Four officers had serious mental changes during atabrine levels of the fourth week. One required confinement in the closed psychotic ward; a second was considered for similar treatment;

and two others were sufficiently confused to require temporary relief from duty. All returned to normal with the cessation of medication. (b) Nineteen of the other officers exhibited the minor cerebral and gastro-intestinal stimulations reported by other authors.

Of the six controls, three developed six temporary scotomas (3 each with 1/ and 6/2,000/white) during the 2nd and 3rd weeks after a positive blood-alcohol level.

Part II: Procedure

Atabrine was discontinued on the 29th day. In the period from the 60th to the 74th days, the examinations were repeated except for the 3/330 perimetries (equipment crated) and the check of refractive errors.

Findings

All but five of the scotomas developed during Part I disappeared. The remaining scotomas were unchanged and were found in three individuals.

Part III: Procedure

Atabrine was recommenced on the 125th day, when approaching the tropics: 0.2 gm. daily for seven days was administered, followed by 0.1 gm. daily throughout the stay in the tropics. The same expert technicians and equipment were used, and the illumination was carefully reduplicated and checked with a light meter.

The basic examination, except for the refraction portion, was repeated in the period from 243rd to the 317th days, when it was considered that the investigation was of sufficient duration for definitive impressions to have been established. The earlier final determinations were necessitated by the impending separation of the individual from the organization for duty elsewhere.

Findings

Of 36 officers completing this section, 6 new scotomas of the previously found average size were present in three subjects. There were no other changes from the normal.

Summary and Conclusions

An investigation of the effects of atabrine upon the human visual system was completed under advantageous circumstances. The blood-atabrine group levels rose to a calculated 79 gamma per liter under circumstances not to be expected in clinical practice.

Scotomas and blind-spot enlargement of minor importance accompanied the suddenly attained high blood-atabrine levels and disappeared with the lowering of the levels.

No other changes occurred in the human visual system during brief or prolonged atabrine administration.

There were no visual-system contraindications to the use of atabrine.

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Grateful recognition of the assistance of 1st Lt. Erleen F. Jamison (A.N.C.), Tech. Sgt. Carl J. Ryan, and T/3 Harold A. Skeem is hereby made.

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DUST-BORNE INFECTION IN OPHTHALMIC SURGERY*

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Asepsis in ophthalmic surgery has long been a problem peculiar unto itself. Of late years, there has been a tendency to conform more closely to the ideas of general surgery—such as the wearing of rubber gloves. But the incidence of infection still remains only slightly altered.

It is well known that by no possible method can the conjunctiva be rendered completely sterile. The discussion concerning the value of cultures taken before operation still finds proponents on both sides of the question. Fortunately for surgery upon the eye, the lysozyme of the tears shows a high bactericidal potency, and the lacrimal apparatus is so constructed that the wounds made at operation are constantly bathed in tears following these operations.

The wonder is not that there is still a certain percentage of infection, but rather that the incidence is so small. This fact, however, should give no grounds for complacency. There is nothing more harrowing in the experience of the ophthalmic surgeon than the discovery of an eye bathed in pus at the first postoperative dressing. Even with all our recent advances in bactericidal drugs and therapy, seldom, indeed, can such a situation be saved. It, therefore, behooves us to search in every direction for any additional precautions that may prevent such tragedies.

During the years of 1926 and 1927, the late Dr. A. E. Ewing was experimenting with various solutions that might sterilize the sharp instruments used in ophthalmic operations without injury to them. By his work, I was stimulated to investigate this problem. My first paper on the subject appeared in the American Journal of Ophthalmology, in 1928.[1] The second was presented before this society in 1940,[2] and the third, written in conjunction with Mr. William Moor, was published in the American Journal of Ophthalmology in 1942.[3] For reasons elaborated in the second paper, the most practical, all-around satisfactory method of accomplishing the desired results appeared to be by means of chemical solutions. That recommended in the last of these three papers, known as No. 4, has been in use by the Department of Ophthalmology of Washington University in all eye surgery since about February 1, 1941. The formula may be written:

Liquor cresolis compound	8.0 c.c.
Oil of lavender	2.0 c.c.
Thymol crystals	2.0 gm.
Ethyl alcohol 95%	88.0 c.c.

Mr. Moor and I were able to demonstrate by experiments recorded in that paper that clean instruments contaminated by cultures made up of various types of virulent organisms could be sterilized by immersion in that solution for a period of one-half minute. Four and one-half minutes, however, were required to sterilize similar instruments, previously soiled by blood and serum, when subjected to the same cultures, plus a heavy concentration of spore-bearing hay bacilli.

It was demonstrated that knives, dropper bulbs, and the like, immersed in this solution for very long periods of time, suffered no deterioration. Three knives, referred to in the third paper, have remained in it since November 14, 1940. They show no dulling of the edges, nor

*From the Department of Ophthalmology, Washington University School of Medicine. Read at the eighty-first annual meeting of the American Ophthalmological Society at Hot Springs, Virginia, November, 1945.

injury to the handles other than an increased translucency of the ivory of one of them. The aluminum and the nickel-plated brass handles of the other two show no change whatsoever. Nor has there been any electrolytic action among the three, despite close contact throughout this long period of immersion. Two rubber bulbs were likewise unaffected in any way after 2½ years. Nor have any of the undesirable effects upon aluminum, encountered in the use of the germicide recommended in the second paper, in which formaldehyde was one of the constituents, been encountered with this solution.

During the past summer, and especially during the month of September, several infections having occurred in the eyes of patients operated upon for cataract in McMillan Hospital, of the Washington University School of Medicine, it seemed desirable to recheck the tests previously made, this time under operating-room conditions, and, also, while studying the action of the germicide, to conduct other experiments with a view to a determination of where contamination might be taking place, should it prove that the sterilizing solution was acting in a satisfactory manner.

Consideration of all the possibilities shows that such infections take place through: (1) contamination residual in the conjunctiva, glands of the lids, lacrimal apparatus, skin; (2) the hands and gloves of the surgeons, assistant, and nurses; (3) droplet infection through the masks of the participants; (4) dust-borne organisms.

This paper, as indicated by the title, does not purport to deal with any of the first three sources, but does attempt to study the fourth route of infection and to point out possible measures that may be instituted to combat contamination of this nature.

For a better understanding of the various stages through which the instruments pass in these experiments, it might be well to note the procedure formerly practiced in our operating rooms. The towels and dressings were sterilized in the usual steam sterilizers. They were then laid upon tables and covered in the usual manner until ready for use. The instruments were first placed in two porcelain dishes, approximately 8 in. long by 5 in. wide, filled with solution No. 4 to a depth of about 1 in. They were allowed to remain there for from 5 to 15 minutes, after which they were passed through a water bath in a similar porcelain dish. No particular effort was made to cover any of these vessels. Following the water bath, the instruments were laid on towels, from the sterilizer, where excess water was removed, the towels, of course, becoming more or less damp as the last ones were dried. They were then placed upon the operating table.

For the purpose of these experiments, instruments of all sorts were removed at all stages of the procedure, as well as from the operating tables, at the close of a number of operations, and tested by immersion in sterile broth cultures. Care was taken not to open and close scissors, needleholders, clamps, and like instruments when introduced into the bactericide, as it was felt that this precaution would often be omitted by the nurses under the pressure of heavy schedules. It may be noted here that, despite this omission, all instruments were found sterile when tested directly upon removal from this solution.

In the first of these five experiments, all shown in table 1, four instruments, taken directly from the germicide, were cultured. In the second, four more were tested upon removal from the water bath, which had stood for some time uncovered on the preparations table. The cultures

from the first four were all negative after 96 hours. Those from the second four were all positive after 24 hours, definitely showing contamination of the water bath. In the third experiment, the water bath was poured immediately before use and thereafter kept constantly covered. Four instruments cultured upon removal from this bath gave negative results after 96 hours. The fourth experiment shows the results obtained from the tests run upon profusion on all plates exposed in the operating room from time to time, indicating air-borne organisms as the source of these contaminations.

It would seem from these results, with 36.23 percent of instruments prepared for operation contaminated even after great care concerning the protection of the water bath had been adopted, that the procedure followed in our operating rooms, at least, was inadequate. And the

TABLE 1

COMPARATIVE TESTS MADE UNDER OPERATING-ROOM CONDITIONS

	Number of Instruments	Hours Cultured 24	48	96	Percent Positive
Experiment 1 Instruments cultured from sterilizing solution	4	−	−	−	0
Experiment 2 Instruments cultured from exposed water bath	4	+	+	+	100
Experiment 3 Instruments cultured from unexposed water bath	4	−	−	−	0
Experiment 4 Instruments cultured from dry towels	4	−	−	−	
	2	+	+	+	
	1	−	−	+	42.86
Experiment 5 Instruments cultured from wet towels	5	−	−	−	
	1	+	+	+	
	1	−	−	+	29.60

instruments taken from dry towels, four on one day and 3 on another. From these seven instruments, four cultures remained negative throughout, two were positive in 24 hours, while one was contaminated after 96 hours. In the fifth experiment, seven more instruments were tested upon removal from wet towels, again four on one day and three upon another. Here, five were negative after 96 hours, one was positive in 24 hours, and one at the 96-hour inspection. It is of interest to note that the predominating organism in all positive cultures was the Bacillus subtilis, which also appeared in probabilities are that much the same, or worse, prevail in most institutions. Certainly the indications are that dust-borne organisms have been playing a large part in the contamination of water bath, towels, and instruments. What, then, can be done to reduce the number of such infections? The answer must lie along the line of air sterilization, or, at least, of protection from atmospheric dust. Our hospitals have been woefully slow to put measures directed toward air sterilization into practice, although the benefits of such procedures are well recognized, and have been employed for some time by com-

mercial houses all over the country. Sterilization of the air has been found highly practical and of the utmost economic benefit in canneries, packing houses, and the like. Where the balance sheet is affected, a remedy has been sought and the means found to put that remedy into practice. Where human happiness is at stake, the means has, as yet, not been found to correct the evil, except in a very limited number of instances.

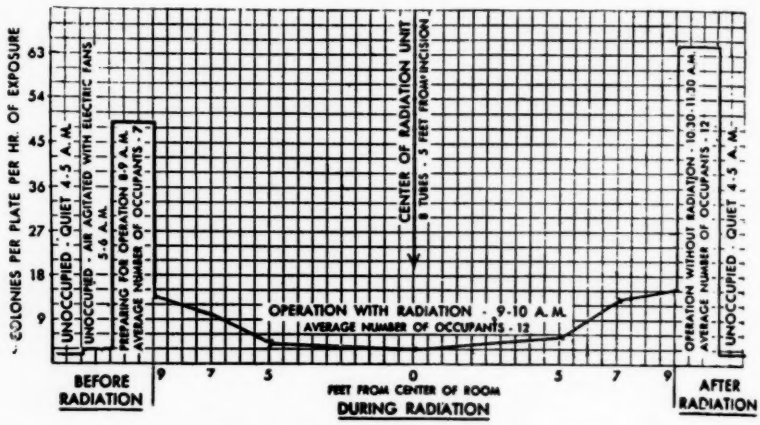

Fig. 1 (Post). Chart showing effect of sterile lamps upon the bacteria content of the air of operating rooms (by permission Westinghouse Lamp Division).

Dr. Deryl Hart,[4] writing from the Department of Surgery of Duke University Medical School and Hospital, upon "Sterilization of the air in the operating room with bactericidal radiation," reported upon results obtained in 132 extrapleural thoracoplasties done under sterile lamps. He found that infection, mortality, and postoperative complications were reduced by half. It is his opinion that contamination of the air can be eliminated almost completely by means of bactericidal radiation. Dr. David T. Smith,[4] from the same department, in discussing Hart's paper, stated, concerning bacteria recovered from the plates exposed in the operating room: "I would not have believed that these were pathogenic bacteria . . . had it not been that organisms so recovered have made very powerful exotoxins which (in one instance) have killed a rabbit in two minutes."

Here, again, in this connection, it is interesting to note that in those infections occurring in our operating rooms last summer and fall, and also one in April of this year, from which cultures were made, large, gram-positive, motile, spore-forming organisms, probably hay bacillus, were recovered, similar to those found in the experiments previously reported.

At present, efforts to sterilize the air are directed largely toward direct action on the air and its dust content by the use, either of so-called sterile lamps or by various bactericidal solutions sprayed into the air. In addition, the effectiveness of either method can be enhanced by the application of oil solutions to blankets, cotton sheets, and floors.

Sterile lamps have been developed extensively and are in use commercially at the present time on a somewhat comprehensive scale. Figure 1, taken from a report of the Westinghouse Corporation of experiments conducted by their laboratories upon air sterilization by sterile lamps, gives a rather startling representation of the effect of these lamps upon the

bacterial content of the air of operating rooms during the course of a busy day. From this graph, it will be seen that the bacterial count, though low at first, while the room was unoccupied, rose enormously during preparation for operation, then fell again almost to its undisturbed state during irradiation, despite continued activity, eventually rising to a still greater height when irradiation was discontinued, although activity in the room remained high, only falling once more to the original condition after several hours of vacancy.

In using sterile lamps, two practices may be employed: (1) The field of operation, tables, and other appurtenances may be subjected to the direct rays from the lamps; or (2) All the air supplying the rooms may be drawn in through conduits over large batteries of sterile lamps, as shown in figure 2, taken from another bulletin of the Westinghouse Corporation. The direct rays from the lamps are of such a nature that they cannot be allowed to fall directly upon the operative field in the case of an eye operation, nor can the surgeons operate under them without protective garments and masks. In addition, the heat generated by a sufficient number of lamps for the purpose would often make them unbearable without air conditioning. The second method of application may be satisfactory, provided ample air conditioning can be secured, as otherwise the heat generated would again be an insurmountable obstacle on many a summer day, when operations must be performed.

The second procedure, that of spraying the air with various bactericidal solutions, gives promise of becoming a practical and satisfactory method under certain conditions. Many investigators are working on this problem at the present time, as the medical personnel of all branches of the Armed Forces are interested because of its bearing upon the reduction of cross infection in barracks and other places where large groups of men are housed in crowded quarters.

In this country, Dr. O. H. Robertson,[5] of the University of Chicago, has been active in these investigations. He, with his associates, working with propylene

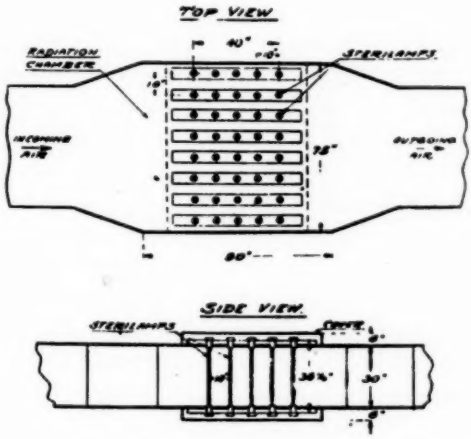

Fig. 2 (Post). Diagram showing how air supplying operating rooms may be drawn through conduits over large batteries of sterile lamps (by permission Westinghouse Lamp Division).

and, more extensively, with triethylene glycol vapor, have shown that 1 c.c. of this substance in 10,000 cu. ft. of air, is lethal to pneumococci, streptococci, and influenza virus previously injected into the air; that, in this concentration, it cannot be detected and is noninjurious to individuals, even after long exposure to its effects. It is most potent, however, at rather high humidity. For instance, the influenza virus survived less than 24 hours at a humidity of 80 to 90 percent, whereas in dry air 25 to 30 percent were recovered after 36 hours.

For its satisfactory use, it is necessary to have control mechanisms and vaporizers. Drs. Puck, Wise, and Robertson[6] have developed a most ingenious, though simple, device, in which control depends

upon variations in the intensity of a beam of light reflected from a polished brass band onto a photoelectric cell, the amount of condensation upon the metallic surface cutting down the stimulus to the cell as the vapor concentration increases in the air, and, on the contrary, permitting greater intensity as the vapor content diminishes. The photoelectric cell may be connected to a vaporizer that can be set up to spray vapor into the air, as called for. Several types of vaporizers have been developed, one by the Research Corporation of New York, and one by Biggs and Jennings[7] of the Technical Institute of Northwestern University.

It is obvious that this method of air sterilization, as well as that by sterile lamps, generates heat and humidity and, for accurate control of the vapor content in the air, requires a closed room, which, in turn, necessitates a satisfactory system of air conditioning for its practical application.

As suggested previously, using either type of air sterilization, the results can be greatly improved by oiling the blankets and sheets. Harwood, Powney, and Edwards,[8] writing in the British Medical Journal for May, 1944, have given detailed instructions for the attainment of satisfactory oiling of these articles. After washing, blankets may be treated in the hospital laundry, using "Fixanol C," a cation-active agent, to deposit upon them a 4.8-percent concentration of oil. Cotton sheets may be treated in a similar way, followed by "Teepol," an anion-active agent, leaving a concentration of 6.7 percent of oil upon these fabrics. Although the results of such treatment cannot be detected by observation or touch, they nevertheless, remain effective for a number of months.

All observers have attributed much of the air pollution to disturbance of the dust upon the floors. It is, therefore, of the utmost importance that some method to hold that dust be instituted. Dr. O. H. Robertson and associates[5] have suggested that pale paraffin oil be used, which will hold dust for many weeks. On tiled floors it may, however, become slippery. Should such be the case, a solution of urea (5 percent), ninol (3 percent), and rocall (0.9 percent) may be substituted very effectively, but must be renewed every few days.

Under present circumstances, air conditioning by either sterile lamps or triethylene glycol vapor is quite impractical in most hospitals, both because of the expense involved and the difficulty in procurement of the necessary equipment. There are, however, a few simple procedures which the author wishes to bring to your attention that are of value in combating infections from these dust-borne organisms. In the first place, all towels, dressings, solutions, and instruments should be protected from dust by sterile covers as much as possible. This is obvious. The second suggestion is to recommend the practice of dipping all instruments which actually enter the aqueous or vitreous chambers into boiling water, or sterilizing solution, for a few seconds immediately before use. Such procedures have been employed sporadically for many years, but I know of no experimental studies that have been made definitively to determine their value. The writer wishes, therefore, to report here a number of experiments which have been carried out with this purpose in mind.

It is well here to point out that this work could not have been done without the assistance and many valuable suggestions of Mr. William Moor, the coauthor of the third paper on this subject. The cultures reported have been taken and read by both of us, working together. The experiments reported earlier in this paper may be considered as belonging to the

first group, and these to the second group.

In this second group, shown in table 2, 18 instruments of various types were taken as a control from eight different operating tables, following their use in operations of one sort or another upon the eye. Cultures taken from these were found positive in 14 out of the total number tested, indicating 77.77 percent contamination at the close of operation. In considering this high percentage, it should be realized that these instruments have been subject to contamination by all four routes previously indicated. It would appear reasonable that if a large proportion of similar instruments taken from these same tables could be sterilized by any method, the procedure employed should be equally, or even more highly, successful in sterilizing those contaminated by dust-borne organisms alone.

The following experiments, reported in table 2, have, therefore, been carried out upon instruments taken from the identical operating tables reported in the foregoing control experiment. The same principle was employed in each instance; namely, dipping the end of the instrument which was to be introduced inside the anterior, posterior, or vitreous chamber of the eyeball into various solutions for varying periods of time, immediately before their use in the operation.

In the first of these studies, the instruments were dipped in water immediately after boiling had ceased. One instrument dipped for 1 second gave a positive culture after 24 hours; 1 dipped for 1½ seconds was positive after 48 hours; but of 4 dipped for 2 seconds, only 2 were positive after 96 hours.

In the second experiment, boiling water was employed. The results, as shown in table 2, were that, of 7 instruments dipped for 1 second, only 1 culture was positive after 96 hours, and of 8 dipped for 2½ seconds, 1 alone gave a positive culture after 96 hours.

It would appear from these experiments that both procedures reduce the percentage of contamination to a very large extent and are well worthy of adoption. The boiling water at one's elbow is, however, somewhat of a nuisance, and on warm days definitely increases the heat and humidity. A solution was sought,

TABLE 2

RESULTS OF EXPERIMENTS CARRIED OUT UPON INSTRUMENTS TAKEN FROM IDENTICAL OPERATING TABLES

Instruments Cultured	Dipping Time seconds	Number of Instruments	Hours Cultured 24	48	96	Percent Positive
Control experiment from postoperative tables	0	14	+	+	+	
	0	4	−	−	−	77.77
Experiment 1						
After dipping in water just below boiling point	1	1	+	+	+	100
	1.5	1	−	+	+	100
	2	2	−	−	+	
	2	2	−	−	−	50
Experiment 2						
After dipping in boiling water	1	1	−	−	+	
	1	6	−	−	−	14.28
	2.5	1	−	−	+	
	2.5	7	−	−	−	12.5
Experiment 3						
After dipping in zephiran 1/3000	2.5	2	−	−	+	
	2.5	31	−	−	−	6.66

therefore, which might be substituted for boiling water; one that would cleanse the instruments without injury to them, or to the eye being operated upon, should occasional droplets be introduced into the eye in the manipulation. In general, the synthetic detergents seemed well suited for such a purpose. Of the 2,000, or more, of these which have been produced, zephiran is one of the most extensively studied and most satisfactory in action. Certainly, its effect upon ocular tissue is well understood. It belongs to the cationic group, all of which are very effective inhibitors of bacterial metabolism at 1/3,000 concentration, and some even at a much greater dilution.

In the third of this group of experiments, therefore, an aqueous solution of zephiran 1/3,000 was substituted for the boiling water. The results, as shown in table 2, experiment 3, were most satisfactory. Of 33 instruments dipped in this solution for 2½ seconds, only 2 cultures were contaminated after 96 hours, that is, 6.66 percent, a considerably lower figure than that obtained in either of the two previous experiments with water baths. Furthermore, though all members of the staff have been asked to watch carefully for any deleterious effects traceable to droplets of this solution being carried into the eyeball upon instruments, none have thus far been brought to my attention, even though due to error a 1/300 concentration was used for about one month.

As previously noted in experiment 2, of the first group, the water bath was highly susceptible to contamination. The satisfactory results obtained by dipping the instruments into the zephiran bath suggested that a similar solution might be used for the removal of the original germicide No. 4 from the instruments, instead of the water bath. A fourth experiment, shown in table 3, was, therefore, carried out, to determine the time that an aqueous solution of zephiran 1/3,000 concentration would remain sterile during exposure to the air in a tray similar to that used for the water bath. Five minims of this solution was removed from the tray at intervals, as shown in the graph, and dropped into culture tubes. As long as the experiment continued, five hours, no positive results were obtained.

To reinforce the findings of this procedure, five instruments were cultured which had just been sterilized by immersion for five minutes in the germicide No. 4, and then washed off in the zephiran bath, as shown in experiment 5, table 3, allowing the bath to stand exposed for 30 minutes. Five more instruments were

TABLE 3

RESULTS OF EXPERIMENTS TO DETERMINE EFFECTIVENESS OF ZEPHIRAN 1:3,000*

	Minutes Exposed	Hours Cultured 24	48	96	Percent Positive
Experiment 4					
Aqueous solution of zephiran 1/3,000 cultured after exposure to air for	0	–	–	–	0
	15	–	–	–	0
	30	–	–	–	0
	60	–	–	–	0
	120	–	–	–	0
	300	–	–	–	0
Experiment 5					
Instruments cultured from aqueous zephiran 1/3,000 after exposed to air for	30	–	–	–	0
	90	–	–	–	0

* All instruments first sterilized by immersion for five minutes in solution No. 4.

similarly treated, after the bath had stood exposed for 90 minutes. As was to be expected, in both instances the cultures remained sterile.

Summary

The conclusions to be drawn from the experiments reported here are, therefore:

1. Keep covers on all solutions, towels, instruments, and the like, as much as possible.

2. Substitute an aqueous solution of zephiran, or some similar detergent, for the water bath.

3. Dip all instruments that are actually to enter the eyeball into a suitable sterilizing solution, or boiling water, for at least 2½ seconds immediately before use.

4. Install, as soon as practicable, some method for air sterilization in the operating room.

5. Treat all blankets and sheets with some type of oil solution.

6. Treat the floor of the operating room with some type of dust-allaying preparation.

In closing, it may be of interest to note that since these investigations started, approximately 600 intraocular operations have been performed, yet only one instance of infection has occurred, and in this case the precaution of dipping the instruments immediately before use, through a misunderstanding, was not observed.

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Discussion

Dr. William M. James (St. Louis): Dr. Post has been interested for many years in the sterilization of the sharp instruments used in ophthalmic surgery. It is fitting that he should call our attention to the dust-borne infections and at the same time suggest methods for their control.

The value of sterile lamp irradiation and of spraying the air with triethylene vapor has been reported and will be used when air conditioning again becomes available.

The results of cultures taken by Dr. Post and Mr. Moor from surgical instruments show that the instruments were being contaminated in the uncovered water bath. The incidence was 36 percent, before use and 77 percent after use. By dipping the instruments in either boiling water or in zephiran 1/3,000 the percentage of positive cultures was reduced to 12 percent and to 6 percent. The advantage of using an aqueous solution zephiran 1/3,000 in place of the usual water bath in sterilizing sharp instruments is shown in table 3.

Dr. Post has told me that there has been some rusting of the instruments following the use of zephiran in the water bath. The Alba Company, the producers of zephiran, state that this factor may be controlled by using 0.5-percent sodium nitrite in the zephiran solution.

DR. WILLIAM H. CRISP (Denver): I suppose everything we can do to improve the sterilization of instruments is not only justified but demanded. However, I wonder whether we do not underestimate the capacity of nature for eliminating danger from the more remote sources of infection. I have never seen anything to lead me to suppose that I picked up an infection from the air of a well-conducted operating room. Over most of my professional career, my sterilization of instruments has been done by simple immersion not in actively boiling water, but in water which has been boiling just before I use it and under which the source of heat has been cut off temporarily so that I shall not scald my hands in the process which I use. For the cataract knife, the Graefe knife, the keratome, or any other knife, I simply hold the knife for 16 to 20 seconds in the water under which the gas has just been turned off so that it is at boiling temperature but not actually boiling. I use all the rest of my instruments in the same water at boiling temperature, but no longer actively boiling, for death of bacteria comes below the boiling point. Most killing or cooking processes are accomplished well below the boiling point, so that I am not afraid of the fact that I have had the gas turned off. I believe that nearly all the inflammatory processes which we see after operation in an eye are due to some variation in surgical technique rather than to active infection. I believe the slow inflammatory processes, especially, do not arise mostly from actual infection.

If you have a foreign body on the cornea, that foreign body tends to favor bacterial development. As soon as the foreign body is removed, unless some process of infection has gone very far, the eye usually reacts very kindly toward it. The point being that any foreign material, or any trauma, will favor bacterial infection; but that bacterial infection very generally does not develop unless the tissues have been traumatized in some unfortunate way. I do not believe any operator on the eye ever performs two successive operations in exactly the same way. There are slight variations in technique. Some of these depend upon slight variations in the anatomy of the individual eye, and I believe that the neatest possible surgery, with avoidance of undue trauma to the tissues, plays a much more important part than our extreme efforts to avoid infection. I am reminded of something I was told about the older Pagenstecher, who many years ago, before sterilization was given as much attention as it is today, always passed the cataract knife between his lips just before making the incision. He said this action made the knife go through more easily, and I do not suppose that he had a greater proportion of cases of infection after his cataract operations than most of us at present. The point here is that, under favorable conditions, the eye is extremely resistant to the threat of infection. For one thing, we have the rapid initial flow of the aqueous, which reduces the basis for bacterial development. Our main salvation lies in the simplest and most straight forward possible surgery, with proper respect to the exact anatomy of the eye of the patient we are dealing with. However, I appreciate that Dr. Post has been doing some excellent scientific work in this direction, and I very much respect what he has done.

DR. FRANCIS HEED ADLER (Philadelphia): I should like to call attention to a factor which will become more prevalent in our operating rooms, and that is the dust-borne infections due to air conditioning. In 1937, our new operating room was opened. We had no trouble from

infections until the first hot week of the summer, when the air-conditioning system was turned on. In that week I had two intraocular infections. Cultures of one of the eyes showed colonies of Bacillus subtilis and the contamination was traced to the air in the room, which was heavily laden with the hay bacillus. It was discovered that the air which came through the system was passing through a chamber loaded with dust and hay bacilli. Dr. Wells and Dr. Stokes have solved our problem by spraying the ducts through which the air is pumped with triethyl-glycol; since then we have had no further infections.

Dr. Arthur M. Yudkin, (New Haven): It is evident from the investigation of Post that dust-borne infection is of great importance in ophthalmic surgery. Although I have not encountered many postoperative infections of the orbital tissue in muscle operations, cataract extractions, operations for glaucoma, or detachment of the retina, I know that some ophthalmic surgeons have been concerned about the frequency of postoperative infections. From 1939 to 1945, when it was most difficult to obtain well-trained assistants in the operating room and the operating teams were overworked, we were free from postoperative infections. It was not unusual for an eye operation to follow an abdominal operation, yet with ordinary care no infections of the ocular tissue were observed.

It is a miracle why more infections are not encountered postoperatively in ophthalmic surgery, for the conjunctiva cannot be sterilized properly, and it is extremely difficult to free the air from air-borne infection. We observe the same operating room technique employed by the general surgeon. The noncutting instruments, towels, gowns, basins, dropper bottles, and table covering are autoclaved under pressure. The medication is sterilized by the drug department daily. The cutting instruments are placed in Post's original sterilizing solution for 5 to 10 minutes.

Post's recommendation of a system of lamps to sterilize the air-borne infection is commendable, and I believe the operating room of the future will be air conditioned and constructed so the air can be sterilized. Not only should the floor of the operating room be prepared with a dust-allaying preparation but the whole operating suite should be protected. The clothing of the operator and assistants should also be considered as a source of contamination. I am satisfied that too many precautions cannot be taken to make an operating field free from extraneous infection. It is important that the operating team and the patient be comfortable in this ideally constructed operating suite of the future.

Dr. M. Hayward Post (closing):

I agree with Dr. Crisp, and realize the truth of his remarks. Our experiments have demonstrated that the eye has a tremendous capacity to fight infection. They show that, though we had 77.77 percent of contamination at the close of operation, yet the hospital records in the past have shown relatively few infections, about one tenth of 1 percent, with approximately 600 intraocular operations performed annually. However, if we can reduce that percentage to nothing, we are making a definite advance. I might also cite in this connection, the experience we had when Colonel Smith demonstrated his intracapsular operation for us on 42 cataracts in one afternoon. During those operations, he smoked no less than four cigars; there were various complications, but no infections.

I attribute the lack of infection at the hands of the older operators to the fact that they were careful not to touch the tips of their instruments, and that they used fewer instruments; consequently, each one could be laid back carefully, so that its tip was not touching anything that might cause contamination.

As to Dr. Adler's remarks, I would say that I have read merely an abstract of my paper. In the complete paper, air sterilization by triethylene glycocoll and ultraviolet is discussed, and ways suggested in which they may be used with safety. Much has still to be done on that subject before the answer is known.

NOTES, CASES, INSTRUMENTS

VENOUS PULSATION AS A SYMPTOM OF EARLY GLAUCOMA*

SAMUEL ENGEL, M.D.
San Francisco

The phenomenon of pulsation of the retinal vessels is usually looked upon as only a curiosity without much clinical significance. Arterial pulsation is present in glaucoma at a pressure of about 60 mm. Hg (Schiøtz). The artery is compressed in diastole, while the vessel is still able to fill in systole, at which time the arterial pressure is slightly higher than the intraocular pressure. Among medical diseases, arterial pulsation is found in aortic insufficiency as a manifestation of the increased pulse-volume, and in Graves's disease.

Venous pulsation as a physiologic phenomenon can be seen in a considerable number of patients, particularly in children. It is due to the fact that the venous pressure is about equal to the intraocular pressure, and the increased filling of the choroidal arteries in systole raises the intraocular pressure just enough to compress the vein, which dilates again in diastole. The appearance of venous pulsation depends, therefore, on the intraocular pressure and on pressure in the vein. In the majority of patients, it can be brought about by increasing the intraocular pressure by pressing slightly on the eyeball. When the pressure is further increased, venous pulsation may be present even together with arterial pulsation.

Increased intracranial pressure, by compressing the vein in the subarachnoid space surrounding the optic nerve, causes stasis in the retinal veins and so raises the pressure in the veins. Absence of venous pulsation is, therefore, an early sign of papilledema. Manz (1874) and Laqueur (1877) observed that venous pulsation is usually lacking in "inflammation of the meninges" with marked venous hyperemia of the retina (cited by Leber[1]). In neurologic patients suspected of cerebral disease, I am inclined to regard the presence of venous pulsation as a sign which makes increased intracranial tension highly improbable, a fact also stressed by Baurmann.[2]

While examining several patients for refraction or because of slight discomfort, I was impressed to observe marked venous pulsation in one eye which was not, or only to a lesser degree, present in the other eye. The pulsation had a slightly different character from the type usually seen. It was more "jumpy;" the constriction was more marked; and the filling more rapid. When taking the tension of such an eye, I found an increased intraocular pressure in many cases. Physiologic variations in the appearance of the venous pulsation were present, and

* From the Department of Ophthalmology, Stanford University Medical School.

I did not find increased tension in all suspected cases. However, those which showed an increase in tension might have been overlooked if my attention had not been attracted by the pulse phenomenon.

Case reports

Short reports of three histories follow:

Case 1. Dr. S. K. D., aged 60 years, came to me in February, 1943, because he felt a slight pain in the right eye when coming from the light into the dark, also after lighting a match in the dark. Examination showed vision to be: O.D., with a +1.25D. sph., 20/15; O.S., with a +1.50D. sph., 20/25. The left eye had always been the poorer eye. The pupil of the right eye was slightly larger than that of the left; the anterior chamber deep. There were two tiny precipitates on Descemet's membrane. The discs were normal, but showed a marked venous pulsation, with the aforedescribed "jumping" characteristics in the right eye. There was a slight venous pulsation in the left eye. The intraocular pressure was 40 mm. Hg (Schiøtz) in the right eye; 20 mm. in the left.

A diagnosis of serous iridocyclitis, with increased intraocular pressure, was made, and the right eye treated with mild mydriatic drops. The tension dropped slowly to 23 mm., and the pulse phenomenon decreased in intensity until it was the same as in the left eye.

When the patient had a similar attack in October, 1943, the degree of venous pulsation made it possible to assume approximately a rise or fall in tension, which was confirmed by the tonometer.

Case 2. Mr. A. W. E., aged 72 years, was seen in October, 1944, for refraction. Examination disclosed vision to be: O.D., with a −1.00D. sph. ⌒ 1.50D. cyl. ax. 15°, 20/40; O.S., with a 1.25D. cyl. ax. 165°, 20/15. (Vision in the right eye had always been impaired.) The iris of the right eye showed a small peripheral coloboma at the 5-o'clock position and some fine posterior pigment synechiae. Gonioscopy revealed that a small tissue stump had been left peripheral to the coloboma and that there were anterior peripheral synechiae on both sides of the coloboma. As the patient had never had his eyes operated on, this condition was assumed to be a coloboma after early inflammation of the iris.

The pupils reacted to light, although slightly irregularly in the right eye. The discs were normal. The vessels of the right eye showed slight bending, which could have been regarded as within physiologic limits. But the central vein of the right eye had a strongly accentuated pulsation, whereas the pulsation in the left eye was just visible. The tonometer registered a tension of 33 mm. Hg (Schiøtz) in the right eye; 23 mm., in the left.

Under treatment (2-percent solution of pilocarpine), the tension of the right eye dropped to normal, and the difference of pulsation between the two eyes disappeared.

Case 3. Mr. W. L., aged 42 years, on a visit to California, came to see me in October, 1945. The day before he had had an attack of cloudiness over the right eye after an afternoon's exposure to sunlight. For the past year, he had experienced similar attacks, but of lesser degree, two or three times monthly. Ten years before, holelike changes of oval form in both maculas (from solar radiation?) had been observed. This had impaired his vision as follows: O.D., with a −4.00D. sph. ⌒ −0.50D. cyl. ax. 90°, 20/25; O.S., with a −0.50D. cyl. ax. 90°, 20/30.

The right eye, whose anterior chamber was deep, showed neither corneal edema nor precipitates. Both discs were normal. A venous pulsation, "jumpy" in char-

acter, corresponded to a tension of 42 mm. Hg (Schiøtz), which decreased to 26 mm. under pilocarpine treatment. Tension in the left eye had always been normal.

On a search through the literature only one reference was found, that of Troncoso, who mentioned, as an ophthalmoscopic symptom of glaucoma, that: "the veins frequently show spontaneous pulsation." It would, therefore, seem worthwhile to draw attention to the fact that a *difference* of venous pulsation in the two eyes, particularly if "jumpy" in character, may be a sign of an early glaucoma that does not yet show marked clinical symptoms and should induce the physician, if for no other reason, to test ocular tension.

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CORNEAL INSULT FROM PODOPHYLLIN

ROBERT S. ROSNER, M.D.
Cleveland

Ophthalmologists must constantly advise doctors against treating skin conditions around the eye as they would elsewhere on the body. The following case points out that doctors have yet to learn this simple dictum.

A practitioner of medicine treated a patient for "warts around the left eye" with a 25-percent solution of oleoresin podophyllin in mineral oil. He stated that this medication was used for the removal of warts in other regions of the body with good results.

Report of a case

A white man aged 52 years, in good general health except for a rectal condition for which he consulted his doctor, was advised by the same doctor to have some warts removed from the region of his left eye for cosmetic reasons. The patient was given a prescription for 25-percent oleoresin podophyllin in mineral oil to be applied nightly with a glass rod to the affected parts. On January 27, 1946, the patient applied this medication to the areas as instructed. No ill effects resulted from the first application. The following night his son applied the medicine to the parts with a glass rod. The patient went to bed soon after, and, during the night, his nose "ran like water," and his left eye smarted and itched. He said that he had not been conscious of any seepage of the medication into the eye but felt that this must have occurred while he slept. Twice during that night he awakened because of some discomfort around the left eye. The next morning the left eye was "all red and puffed up." Some discomfort was present, but no severe pain. He was able to stay on his job by squinting and keeping the left eye closed. When the eye was opened, he felt some pain. He consulted the practitioner on January 29th, because the pain grew progressively worse. An analgesic ointment was instilled, and the eye bandaged. The doctor instilled more ointment on the following morning. The patient then became aware that vision in the involved eye was

extremely blurred, although the pain had somewhat abated. He was sent to the writer for consultation on January 31, 1946.

OPHTHALMOLOGIC EXAMINATION

Visual acuity was 6/6 in the right eye, and 1/60 in the left eye. On the skin of the temporal half of the lower lid of the left eye were multiple small papillomatous growths; a few were on the upper lid also. There was dryness and excoriation of the skin around the outer canthus. Moderate photophobia was present. The bulbar and palpebral conjunctivas were congested and edematous. Ciliary venous congestion was marked. There were considerable lacrimation and some bhepharospasm, which were somewhat relieved by the instillation of a 0.5-percent solution of pontocaine. A 2-percent solution of fluorescein was applied, followed by another drop of pontocaine. An irregular rounded corneal ulcer took the stain. This ulcerated area, located directly at the center of the cornea, was about 4 mm. in its widest diameter. There were also two other tiny ulcers near the limbus, one at the 11-o'clock, and the other at the 5-o'clock position. The entire corneal epithelium was strikingly hazy and lusterless (see figure 1).

Slitlamp examination. The edema of the epithelium was seen chiefly by retroillumination. It had the appearance of tiny globules of varying sizes. The ulcer, discform in appearance, was superficial, amounting only to a loss of surface epithelium. No erosions were present in Bowman's zone, and there was no corneal vascularization. The vascular plexuses at the limbus were greatly congested. Many tiny, rounded spots of infiltration in the corneal stroma extended down to Descemet's zone. The most remarkable finding was that Descemet's membrane was wrinkled throughout the entire posterior corneal surface. No keratitic precipitates were present. There was a one-plus aqueous ray, but it was assumed that this was caused by diffraction of light by the translucent and hazy cornea. Even with the use of a high-power lens, no cells were seen in the anterior chamber. However, it was difficult to penetrate the corneal haze. The iris showed no involvement.

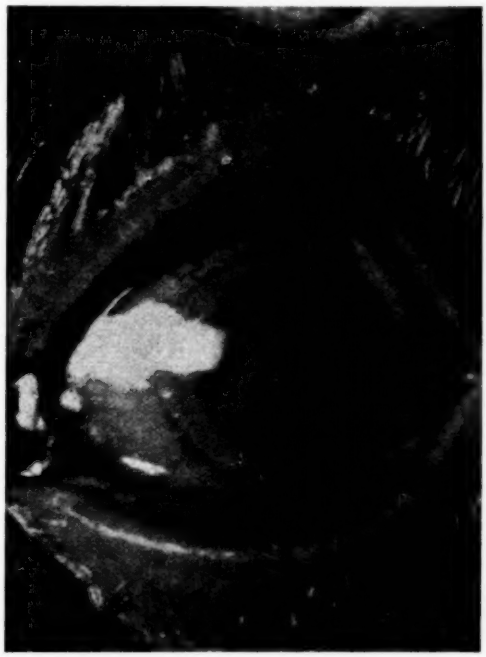


Fig. 1 (Rosner). Corneal lesion as the result of the use of oleoresin podophyllin in the region of the eye.

Ophthalmoscopic examination. Only a red reflex could be obtained in the left eye. No details whatever were visible. The right eye was entirely normal. A 3-percent solution of homatropine was instilled into the left eye. This was followed by the application of holocaine-epinephrine ointment and an eye pad. The patient was observed daily. On the third day, the ulcer had healed, and the area did not take the fluorescein stain. Vision had improved to 4/60. Although the pain had subsided

completely, one could not obtain a view of the fundus. Descemet's membrane was still wrinkled in a peculiar wire-screen or checker-board fashion which was most noticeable near the center of the cornea. The corneal periphery was clearing well. Even though the anterior chamber was not entirely clear, there was no aqueous flare. High-power examination failed to reveal any cells. Treatment consisted of frequent instillations of sterile olive oil. The eye pad was removed. On February 8th, the cornea had cleared sufficiently for the patient to be able to read the 6/9 line. However, even though they were fading, the criss-cross folds in Descemet's membrane could still be seen.

Outcome

Not until one month after the onset of this disturbance did the eye become totally quiet. Grossly, one could see a faint, nebulous scar at the center of the cornea. Vision in the left eye was corrected to 6/7.5−2. Slitlamp examination revealed that the wrinkles in Descemet's membrane had disappeared completely. The nebulous region was carefully studied. It consisted of extremely fine, silvery dots and spots scattered throughout the substantia propria of the cornea. Bowman's and Descemet's zones were not involved in this process. A good fundus view was obtained, and the fundus was entirely normal.

Conclusion

A case of corneal insult from oleoresin podophyllin has been presented. One cannot help but marvel at the recuperative powers of the cornea. Despite this fact, ophthalmologists should warn the general practitioner of medicine to treat skin conditions around the eye with utmost caution.

707 Rose Building (15).

SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

November 5, 1945

DR. PERCY FRIDENBERG, *presiding*

IONTOPHORESIS IN OPHTHALMOLOGY

DR. LUDWIG VON SALLMANN presented a paper on this subject during the instructional hour.

GENERAL ANESTHESIA IN OPHTHALMIC SURGERY

DR. MORRIS BIEN gave a report on this subject which has been published in this Journal (September, 1946).

Discussion. Dr. James W. Smith said that some slips in technique are seen in the general hospital which nullify the anesthetist's efforts. Preoperative orders for children are not always followed, and the operation may be interrupted by vomiting of orange juice or food given before operation, usually by a comrade. He said that he has observed marked cyanosis in children after operation when the nurses failed to remove the endotracheal airway. When pentothal anesthesia is employed, adequate local anesthesia must be used because there may be pain, especially in muscle surgery.

Dr. Joseph J. Fried described a case in which pentothal was used for an iridectomy. When the iris was grasped, the patient sat up and sneezed; this was repeated after a few minutes wait. Another patient, given pentothal for an enucleation, remained unconscious for three days. The diagnosis was respiratory depression from the anesthesia. Within a few days, a fatal hypostatic pneumonia developed.

Dr. Benjamin Esterman inquired about the dosage of atropine as premedication for ether anesthesia.

Dr. Bien said that he has experienced the same difficulties which Dr. Smith described. He avoids very deep anesthesia in children, tries to anticipate the end of the operation, and stops the anesthesia early so that, by the time the eye is dressed, the reflexes are returning and the airway can be removed in the operating room.

The average dose of atropine for an adult is 1/150 gr. However, the dose varies with the patient. A 16-year-old patient would receive 1/200 gr. together with 1/8 gr. of morphine.

The best time for administration is one hour before operation when given in conjunction with an opiate, and one-half hour before if given alone.

LOCAL ANESTHESIA IN OPHTHALMOLOGY

DR. WALTER S. ATKINSON attributes many operative accidents to forcible contraction of the orbicularis or to failure of the patient to hold well because of incomplete anesthesia. Many cases of vitreous loss are due to poor anesthesia and, if more than one percent of uncomplicated cases lose vitreous, the anesthesia procedure should be checked.

A patient's confidence is an important factor which sedatives aid in achieving, but sometimes sedatives produce excitement, nausea, or vomiting. Administrating them the night before operation will indicate the patients who react adversely. For preoperative use, phenobarbital or pentobarbital, 1.5 gr. or more, with aspirin, 5 gr. (the latter apparently has a synergistic action), is effective. Tetracaine (pontocaine) 0.5 percent is the most suitable of the surface anesthetics. Procaine (2 percent with 1 drop of epinephrine 1:10,000 to 5 c.c.) is also effective. The epinephrine is raised to 4 drops for

retrobulbar anesthesia when it is desireable to lower intraocular pressure. A luerlock syringe is the most satisfactory type. Needles recommended are: no. 27 (12.5 mm.) for subcutaneous use; no. 25 (2 cm.) for akinesia and deeper subcutaneous injection; and no. 22 (3.5 cm.) for retrobulbar and deep injection.

The O'Brien lid block seems more efficient than the Van Lint. In performing this, have the patient open his mouth to permit identification of the condyloid process, introduce the needle almost to it, inject a few drops, advance to the process and inject 2 to 3 c.c. If akinesia does not take place in a few minutes, another injection is indicated.

It is advisable to produce a dermal wheal prior to retrobulbar injection which should be done with a 3.5 cm. needle having a rounded point. If the patient looks up and away from the site of injection, the fascial connection of the muscles will be drawn away. As long as the needle is within the muscle cone, anesthesia will be satisfactory because the solution diffuses throughout the fatty tissue. For operation on the globe, 1 to 1.5 c.c. is injected, and 3 c.c. for enucleation or muscle operations. This will block the sensory nerves and produce paresis of the rectus muscles which reduces the likelihood of squeezing. The anterior chamber will be deeper; the lens capsule will be looser; and the possibility of vitreous loss will be diminished. Concurrent instillation anesthesia is required since only the conjunctiva about the cornea is anesthetized. Retrobulbar anesthesia is also useful in lowering pressure and relieving pain in acute glaucoma.

For lacrimal sac operations, the infratrochlear nerve is blocked by inserting the needle to a depth of 3 cm. at the upper-nasal angle of the orbit. Another 0.5 c.c. is injected at the supra-orbital notch. To produce anesthesia of the duct and lower sac, the infra-orbital nerve is blocked by inserting the needle in the canal, which is 1 cm. from the ala of the nose, and injecting 1 to 2 c.c. If there is no foramen, or if it is missed, the injection is made at the infra-orbital fissure.

Tumors of the lid are removed under infiltration anesthesia except in cases when they are so large that they require block anesthesia. This is produced by injecting along the orbital margin, carrying the needle close to the bone to beyond the horizontal borders of the lid.

Discussion. Dr. Max Kimbrig described one case in which the pupils dilated after the use of tetracaine. He thought there had been some error made and reinstilled the drug at a later date with pupillary dilatation again taking place.

Dr. Harvey Thorpe said that occasionally patients will be given tetracaine for treatment of corneal ulcers or other conditions. Sometimes the eye becomes sensitive to this drug, and a corneal ulcer develops which takes many weeks to heal. He considers the retrobulbar injection of novocain of great value as it softens the globe and minimizes vitreous loss. The needle should be examined before use. A damaged point may tear an orbital venule and result in retrobulbar hemorrhage. Placing the finger between the globe and lower orbital margin, thereby pushing the eye upward, facilitates the passage of the needle behind the globe.

Dr. Atkinson stated he had never seen a case of dilatation of the pupil with tetracaine.

Pharmacology of ophthalmic drugs

Dr. Walter Modell stated that the conjunctiva are excellent absorbing surfaces. Lowering the surface tension speeds their absorption. The wetting agents or detergents which accomplish this often are quite irritating, but the aerosols and zephiran, in proper concentration, can be used safely. The closer the

osmotic tension to isotonicity with the tears, the more rapid the absorption. Tables indicate the amount of salt required for various drugs. Most ophthalmic drugs can be buffered to slight alkalinity at which they are absorbed best by the conjunctiva. The closer alkalinity is to pH 7.5, the less is the irritation.

The sulfonamides and penicillin have resulted in new standards of antibacterial effectiveness. A chemical antiseptic, by definition, retards the development of disease-producing bacteria in vitro, but the in-vitro characteristics have no bearing at all on an antiseptic's usefulness in treating infections on the surface of the eye or in the body, and some interfere with the body's normal anti-infective actions. They may be mutually antagonistic with the lysozyme of the tears, vitiating the antibacterial properties of each other. In general, sterile wounds heal more rapidly if antiseptics are not applied and, in infected wounds, strong chemicals seem to retard the eradication of bacteria. It is doubtful if local infections in the eye are exceptions to this rule.

Experience has shown that the local use of sulfonamides is not as effective as originally believed. All evidence indicates that they work from the interior of the cell and not as surface-acting materials.

Penicillin is surface active and well-absorbed by the eye. It is effective by injection and orally but about five times as much must be taken by mouth for effects equivalent to those produced by intramuscular injection. The blood level must be maintained continuously as peaks represent wasted penicillin.

Ophthalmology has, perhaps longer than any other branch of medicine, made use of drugs acting on the vegetative nervous system. The choline group is one of the recent parasympathetic-affecting additions to this list of drugs. Their action in the eye simulates stimulation of the oculomotor nerve which normally functions by elaboration at the nerve ending of acetylcholine which in turn is destroyed by cholesterinase. Acetylcholine is too quickly destroyed to be useful clinically. Mecholyl, its betamethyl derivative, is much more slowly destroyed and is clinically valuable. Doryl, called carcholine for ophthalmic use, is carbaminoylcholine, and is not destroyed at all by esterase. Its absorption, when instilled in the eye, is enhanced by a wetting agent, for which zephiran is usually recommended.

Physostigmine and prostigmine produce their parasympathetic effect by destroying esterase and permitting the accumulation of the acetylcholine. When administered together, they similarly protect mecholyl.

A new derivative of carcholine, called dibutoline, introduced by Swan, has an increased surface activity and is well-absorbed by the eye. Surprisingly, its action is similiar to atropine, being a mydriatic and a profoundly rapid acting cycloplegic. It is antiseptic, as are all wetting agents. The best explanation for its reversal in action is that it is actually inactive but that it is so similar, chemically, to acetylcholine that the body does not discriminate between the two. If enough is present, it displaces the normally formed acetylcholine and prevents its action.

Discussion. Dr. Fredrick H. Theodore said that he thought Dr. Modell felt that the sulfa drugs were not effective when applied locally to the eyes. He described well-controlled cases which showed the contrary: (1) An occlusion body conjunctivitis that had not been treated for one month. Local sulfa treatment resulted in complete disappearance of clinical symptoms and signs in three days. (2) An acute staphylococcus conjunctivitis which cleared up with the local use of sulfonamides alone. Dr. Theodore also remarked on the great frequency of aller-

gic reactions produced by penicillin ointment.

Dr. Adolph Posner pointed out that pilocarpine has been a standby for many years. Only recently have the choline derivatives become popular. With Dr. Mark Schoenberg he developed some criteria regarding their use. It seemed to him that prostigmine or doryl are no better than pilocarpine and probably less reliable in chronic glaucoma. Their effect probably depends on the state of the parasympathetic system at the time of use.

Dr. Modell said he did not question that sulfonamides used locally are effective in the treatment of some infections of the eye. He questioned, however, whether the local use of the drug is superior to adequate oral administration.

Regarding reactions to penicillin, he said that all such reactions may not be due to the penicillin itself. About 50 percent of the parenteral penicillin preparations now on the market have impurities which may be to blame. However, there is reason to believe that, in some cases, pure crystalline penicillin also produces reaction.

Pilocarpine acts to produce parasympathetic effects much like those produced after the administration of physostigmine. It acts directly, however, and not, as does the physostigmine, through an intermediary acetylcholine. Since pilocarpine is more independent in its action than physostigmine, it seems reasonable to suggest that there may be situations in which pilocarpine would produce satisfactory effects while physostigmine or prostigmine would fail.

Recent progress in ophthalmic therapy

Dr. James W. Smith said penicillin is the drug of choice, and effects a more rapid cure than the sulfonamides in the treatment of gonorrheal ophthalmia, penetrating injuries, orbital cellulitis, and ulcerative keratitis. The organisms most sensitive to penicillin are beta-hemolytic streptococci, gonococci, streptococci viridans (alpha), streptococci anhemolyticus (gamma), and some strains of staphylococci.

Penicillin may be applied locally by instillation (500 to 10,000 Ox. u. dissolved in 1 c.c. isotonic sodium chloride or distilled water, pH 7.7), conjunctival pack (20,000 Ox. u. per c.c. concentration), ointment (1,000 Ox. u. per gm.) intramuscularly, intravenously, or orally (calcium-penicillin tablets 20 to 25,000 Ox. u.). Intraocular infections of the anterior segment after penetrating wounds can be treated by withdrawal of 0.25 c.c. of aqueous and replacement by penicillin solution (1,000 Ox. u. per c.c.).

The clinical disorders responding to the sulfonamides are trachoma, inclusion conjunctivitis, lymphogranuloma venereum, gonorrheal ophthalmia, streptococcic corneal ulcer, bacillus pyocyaneous ulcer, erysipelas, impetigo of the lids, and staphylococcic blepharoconjunctivitis.

Sulfathiazole and sulfadiazine penetrate poorly through the cornea. The wetting agents, by lowering interfacial tension, increase the concentration of these drugs in the aqueous humor and make them effective for treating anterior segment infections. Aerozol-os (0.5 percent) is a nonirritating detergent.

Iontophoresis, combined with oral and topical application of the sulfonamides will produce maximum concentration in the cornea, aqueous, and anterior uvea in treating extensive corneal ulcer, endophthalmitis, and panophthalmitis.

Mecholyl, neostigmine bromide (prostigmine), and carcholin (originally marketed as doryl) have added greatly to the medical treatment of glaucoma. Mecholyl

chloride, 10 percent, with prostigmine, 3 percent, is an excellent miotic for patients with chronic simple glaucoma that cannot be controlled with pilocarpine and eserine. For acute congestive glaucoma, inject morphine sulphate (0.25 gr.) and instill mecholyl, 20 percent, and prostigmine, 5 percent (1 drop every 10 minutes for 7 doses). If intraocular pressure is not reduced after 1½ hours, give a retrobulbar injection (25 mg. of mecholyl in 1 c.c. procaine, 2 percent). The antidote, if necessary, is atropine 1 to 2 mg. Continue mecholyl and prostigmine drops for five additional doses. These drops are also recommended as a collyrium every 10 minutes for 1 to 2 hours, preoperatively, to reduce intraocular pressure.

Carcholin is valuable as a "rest therapy," after which the patient may be more responsive to the use of the usual miotics. In a 0.75 percent concentration, it is less irritating than pilocarpine and eserine and does not produce allergic dermatitis or conjunctivitis. Carcholin drops are not surface active. Vigorous massage for two minutes after instillation is necessary to increase absorption and the drug's effectiveness.

Dr. Smith stated that the extravagant claims made for vitamins in ophthalmic therapy have not been substantiated. He prescribes vitamin A for old, feeble patients with recurrent catarrhal ulcers, keratoconjunctivitis sicca, and mild forms of epithelial dystrophy. Vitamin B and B complex are effective in toxic amblyopia and retrobulbar neuritis. Vitamin B_2 is effective in rosacea keratitis. Vitamin D, in combination with vitamin A, is helpful for phlyctenulosis and severe blepharitis in children. Dr. Smith questioned the efficacy of vitamin C. The indications for vitamins K and P are limited.

Considerable progress has been made in decreasing the irritation of eye drops and improving their effectiveness by the use of solutions isotonic with tears, by standardization of the pH, and by the use of buffer solutions.

The detergents or "wetting agents" have been shown to accelerate the absorption of drugs like carcholin and the sulfonamides, but unfortunately these agents have an irritating and deleterious effect on corneal epithelium. Detergents should not be used in eyes with corneal abrasions.

Dr. Smith referred briefly to dibutoline sulfate, the newly described surface-active mydriatic and cycloplegic, which can be used safely in patients sensitive to the to the atropine drugs.

Leon H. Ehrlich,
Secretary.

COLORADO OPHTHALMOLOGICAL SOCIETY

November 17, 1945

Dr. Walter Ohmart, *president*

Drusen of the optic disc

Dr. William M. Bane reported on Mrs. R. H. C., a 38-year-old white woman with general good health. She noticed, six years ago, that the pupil of the right eye was dilated. No cause was found. She was seen by Dr. Riche at that time. Neurologic findings were negative. There was no history of injury. Glasses were ordered 5 years ago, by an optician. Examination: R.E., 5/20; L.E., 5/20. The media were normal. Refraction was performed and glasses were ordered for myopia giving vision of 5/4 in each eye. Each disc was partially covered with excrescenses which are called drusen.

According to Duke-Elder, drusen are really hyaline bodies made up of concentric laminations with no cellular structure nor capsule. They are supposed to be de-

rived, as is Bruch's membrane, from pigmentary epithelium displaced into the disc. Fuchs says they are of neural origin.

The appearance varies from flat masses to grapelike elevated clusters. They are located at the edge, center, or completely covering the disc. The condition is usually bilateral and may be associated with similar formations in the macula or elsewhere. It occurs in all ages but is most common in the aged and in the presence of retinal disease. If pressure on nerve fibers occur, there may be some atrophy and field changes.

ANIRIDIA OR IRIDEREMIA

DR. WILLIAM M. BANE reported on the case of a white boy, aged five years. This boy was seen several months ago at the clinic. Both eyes were similar, exhibiting the typical picture of aniridia, a rare congenital defect in which the iris is not completely absent but only a short rudimentary stump can be observed, hidden behind the cornea-scleral margin. The pupil occupies the whole area of the cornea, and the margin of the lens, the zonular fibers, and the summit of the ciliary processes may be observed. In this case, the lens margins were flattened at the six-o'clock position, indicating, here, a contraction of the capsule where the zonular fibers had probably ruptured. The boy exhibited no evidence of poor vision, and had no nystagmus nor photophobia, which so often accompanies this condition. The anterior chambers were normal in depth, and the lenses were neither ectopic nor cataractous. The history of heredity in this case was negative.

Discussion. Dr. Fritz Nelson and Dr. John Long suggested the tattooing of an iris on the cornea. Dr. W. T. Brinton mentioned a case of traumatic aniridia in which the eye was not sensitive to light. Dr. Morris Kaplan suggested colored contact lenses.

MEDULLATED NERVE FIBERS

DR. WILLIAM M. BANE reported on Mr. C. M. S., age 42 years. His condition, of opaque nerve fibers of marked degree which almost surrounded the disc of the left eye, was shown to illustrate the fact that elevation sometimes is noted. In this case, it measured about 2D. and could be distinctly observed by parallax. Medullated nerve fibers are not observed in the newborn, but develop after birth, and, therefore, are not considered congenital.

MALIGNANT MELANOMA

DR. R. W. DANIELSON presented a report of two cases.

Case 1. J. T. S., a 32-year-old man, who had been seen first in November, 1942, because of cloudiness of vision of the left eye, of two-weeks' duration. Vision was: L.E., 20/20; R.E., 20/15. No lesion of the media or fundus could be found, and the peripheral field was normal although there was a questionable enlargement of the blind spot. He was treated with typhoid vaccine, but by July, 1943, vision was 20/25.

In August, 1944, a faint, dark, choroidal elevation above the left macula was first noted. Vision was 20/25, but no central-field defect could be found corresponding to the lesion. However, by June, 1945, there was a small scotoma near fixation which had enlarged considerably by October, 1945.

At the time of presentation, vision was 20/40. The elevation had increased 1D. in five months. Tension was 20 mm. Hg (Gradle-Schiøtz). There were a few punctated hemorrhages in the retina, especially over the elevation. General examination had revealed no abnormality elsewhere. No foci of infection were found, and the Kahn test was negative. No melanin was present in the urine. The patient was presented for opinions as to the advisability of enucleation.

Dr. Danielson said that no transillumination had as yet been tried because of the scotoma's location but that even if some shadow did show, it would not prove a melanoma. In fact, as was pointed out, there is, as yet, no positive test or manner of examination by which a differential diagnosis between an early melanoma and other lesions of the choroid can be made. It was mentioned that it seemed somewhat ironic to have means of analyzing the composition of stars millions of miles away by spectroscopy, but no way of telling the composition of a structure close at hand. It was thought that someday there might be a device, like radar perhaps, whereby reflected rays might give an inkling as to the content of a tumor. In the absence of such an imaginary device, it was hoped that X ray might be sufficiently refined so that it would help in diagnosis and that the path to progress would lead to the finding of some chemical which, when injected intravenously, would have a selective affinity for melanin and would be radiopaque. If such a chemical could be found, it would also be of value in searching for possible metastases. Perhaps melanin so treated might be mixed in vitro, be injected and be found to have selective affinity for a melanotic tumor which ordinarily produces melanin.

Case 2. Dr. R. W. Danielson also presented R. M. A., a 69-year-old man, who had noticed a progressive loss of vision in his right eye for about a year. He had had no pain or inflammation in the eye. On examination, a large, brownish-black, pigmented mass was found hanging from the ciliary body and anterior choroid superiorly. Tension was 11 mm. Hg (Gradle-Schiøtz). The peripheral field showed generalized contraction rather than an inferior defect, as one would expect. The fundus was normal except in the region of the elevation. The affected area transilluminated very poorly. An interesting feature was the presence of an opacity of the lens capsule near the tumor, similar to the case shown by Dr. Fritz Nelson at the last meeting.

After reviewing some recent literature, Dr. Danielson pointed out the high incidence of death, even when the eye had been removed quite early. He conjectured the possibility that these tumors tend to metastasize in their incipiency, rather than later when, perhaps, some reactive mechanism tends to bind the tumor cells in place. He wondered whether the opacity in the lens is due to pressure, to some toxic action, or to an involvement of the ciliary nerves supplying that part of the eyeball, since malignant melanomata are now thought to have their genesis in neural elements.

Marcus Gunn syndrome

Dr. John C. Long presented the case of J. A. S., a five-year-old boy with a Marcus Gunn syndrome. The boy showed a marked ptosis of the left upper lid. The left lid opened widely when the jaw was opened; especially when the jaw was thrust to the right. Opening of the left lids was much less pronounced when the jaw was thrust to the left. On chewing, there was a rhythmic raising and lowering of the left upper lid. This condition was somewhat more pronounced when the eyes were turned downward. There was also a paralysis of the left superior rectus muscle. The defect had been present since birth.

Herpes zoster

Dr. Muir presented E. H., a white man, aged 76 years. In May, 1945, he had an eruption which, on the right, followed the distribution of the Vth nerve. This eruption was accompanied by pain. When he was seen in the clinic at Grand Junction, June 6, 1945, the eruption was near-

ly gone, but the pain persisted. The patient also complained of diplopia.

Three 5,000-unit dosages of diphtheria antitoxin were given. Four Kahn tests were: (1) positive, (2) positive, (3) doubtful, (4) negative. Spinal test was negative. He was also given alchohol and cocaine injections into the medial aspect of the right eyebrow, which only made the pain worse.

Seen at the Colorado General Hospital for the first time on October 21, 1945, he was referred to dermatology, where he was given six injections (2 c.c. each) of thiamin over a 12-day period. Since the patient still complained of pain, cobra venom treatments were started on November 15, 1945.

Examination at the eye clinic revealed: On November 2, 1945, asymptomatic. Vision was R.E., 20/100; L.E., 20/30, plus. The patient said that ptosis was disappearing, and that there had been no diplopia for a long time. Pain returned on November 13th. The cornea of the right eye showed diffuse, generalized, superficial, punctate staining areas. On November 15th, only the inferior portion now stained. At present the residuals of herpes zoster ophthalmicus are present on the right forehead and eyelid, especially on the palpebral conjunctiva. Both the ptosis and diplopia were transient. Corneal staining recurred after an interval in which the patient was free of ocular symptoms.

Discussion. Dr. Katherine Chapman suggested the injection of pituitary and the local application of collidum. Dr. J. Shields advised the use of penicillin, locally, and Dr. J. Long suggested the use of convalescence serum.

Gertrude Hausmann,
Secretary.

CHICAGO OPHTHALMOLOGICAL SOCIETY

November 19, 1945

PETER C. KRONFELD, *president*

CLINICAL PROGRAM

(Presented by the Department of Ophthalmology, University of Illinois Medical School)

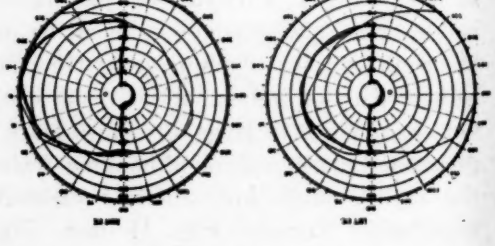
SPASTIC DIPLEGIA WITH HOMONYMOUS HEMIANOPIA

DR. EDWARD J. HORICK said that C. R., a woman, aged 33 years, complained that her eyes tired quickly with near vision. Refraction showed a −3.00 sphere in each eye and a divergence excess, 26 degrees for near. Exercises helped considerably, and she is now comfortable with near work.

Visual field study showed a homonymous hemianopia with sparing of the fixation area. She had been unaware of the defect. The neurologic report was antenatal disease of the brain. The condition may be regarded as a variation of Little's disease.

GROUPED PIGMENTATION OF THE RETINA

DR. STEPHEN W. SUKUMLYN presented M. L., a white boy, aged 17 years, who was referred from the Department of



Pediatrics and Endocrinology where he was studied for obesity. Laboratory tests were negative. External examination of the eyes was negative. Visual acuity was:

R.E., 1.5—2; L.E., 1.5—3. He had never worn glasses.

Examination of the fundi after homatropine refraction revealed normal papillæ and normal retinal vessels. The immediate area surrounding the discs and extending to the temporal side to include the macular region was of normal orange color. In the right eye, toward the nasal side, there were numerous various-sized dots, spheres, ovals, and other irregularly shaped, sharply defined spots of pigmentation gradually increasing in number as they receded from the disc toward the equator. The pattern had a tendency to run in groups, the groups forming a congestion which followed the equator of the eye, becoming more scant on the temporal side. The picture in the left eye was similar, although less striking. The pigment ranged in intensity from light to dark gray, and its position in the retina was below the retinal vessels and above those of the choroid.

Peripheral fields were normal for red, white, and blue; central fields showed no scotomata.

This is a typical case of group pigmentation of the retina. It has normal visual acuity, normal central and peripheral fields, and an abundance of pigmentary plaques in the retina. Comparatively few cases have been recorded in the literature, under various names such as: melanosis of the retina, group pigmentation of the retina; nevoid pigmentation of the fundus, and congenital melanosis of the retina. The explanation of the position of the pigment as given by Ida Mann is "an atypical differentiation of isolated cells of the inner wall of the cup, each of which has developed pigment and then divided to form the small clump of cells seen in the pigmented spot." Parsons, after microscopic examination of such an eye in 1904, explains the plaques as aggregations of deeply pigmented cells of retinal epithelium which found their way into the layers of the retina through spaces where rods and cones had failed to develop.

Bilateral external rectus paralysis (congenital)

Dr. Roosevelt Brooks said that D. V., aged 17 months, was first seen in September, 1944. The mother stated that the child's eyes had always turned in. There was no history of birth injury.

On examination, both eyes turned toward the nose 40 to 45 degrees with little or no rotation externally. The child turned her head to see at the extreme right or left. When looking to one side, there was increased effort to converge with one eye but no noticeable external rotation of the opposite eye. The pupils reacted to light, and the discs appeared normal. No visual findings could be obtained. Attempted refraction under atropine cycloplegia gave: R.E., with a +2.50 D. sph. ⊂ + 1.25D. cyl. ax. 15°. No figures were obtainable for the left eye because of poor fixation.

At the most recent examination, there was definite fixation with the right eye but no external rotation beyond the midline. The left eye still did not rotate externally, and the child cannot fix with this eye. In other words, there has been some improvement in external rotation of the right eye during the year that she has been under observation.

According to Whitnall, congenital factors are largely due to errors in development by cleavage from the common premuscular mesoblastic mass. Harold Gifford reported a series of cases in 1926, including unilateral and bilateral paralysis of external recti. He stated that the defect seemed to be due to hypoplasia or simple lack of development of the nucleus as opposed to the theory of intra-uterine disease. Some of his cases were associated

with other congenital defects, such as reduced adduction, paralysis of the facial nerve or tongue, or defects of the hands. However, no other congenital defects were observed in this case. The closeness of the 6th and 7th nuclei rather speaks for a central lesion. Birth injury is undoubtedly responsible for many supposed congenital ocular-muscle paralyses. The greater frequency of paresis of the left external rectus would lead to the belief that even moderate pressure in the birth canal will explain many cases.

Heredo-familial macular degeneration

Dr. Martha Rubin Folk presented four cases.

Case 1. T. R., a white man, aged 25 years, complained of failing vision which began at the age of 18. Two sisters suffer from the same condition; the vision of the parents is apparently normal.

External examination of the eyes was negative. Vision was: R.E., 0.2; L.E., 0.2. The pupils reacted to light and accommodation. Examination of the fundi showed, in the macular region, a triangular area about one-third disc diameter, with some pigmentary disturbance as a pepper and salt macula. In the center of the macula, a darker pigmented patch was seen. The central fields showed a central scotoma, and the peripheral fields showed a 30-degree contraction for red. Treatment included lextron ferrous capsules and vitamin B_1.

Case 2. B. G., a white woman, aged 42 years, was first seen in September, 1945, with a complaint of gradual loss of vision which began at the age of 14 and was progressively getting worse. She married at the age of 21 and had three children, one of whom had trouble with her eyes. There were mild pigmentary changes in the macula with no loss of vision. The patient has one brother and one sister with similar eye conditions.

On examination, the eyes were negative externally. Vision was: R.E., 16/200; L.E., 0.4. Ocular movements were normal; irides were blue; pupils reacted to light and accommodation.

In the right macula, an atropic lesion with sharp margins was seen. This lesion, about two disc diameters in size, was sprinkled with pigment and gave a salt and pepper appearance. The left macula had a similiar lesion. The red fields were contracted to 30 degrees and also showed a central scotoma. Physical and laboratory examinations were negative. Treatment included vitamin B_1 (5 mgm.).

Case 3. S. K., a white woman, aged 34 years, gave a history of difficulty in reading as far back as she could remember. One sister and one brother had similar eye conditions. The mother and father were unaffected.

Vision was R.E., 0.1; L.E., 0.1. Ocular movements were normal. Pupils were 4 mm. in diameter and reacted to light and accommodation. In the macula was seen an apple-shaped atrophic area with sharply demarcated edges, and with a blood vessel running through the central portion of the lesion giving a salt and pepper appearance. A black-pigmented patch on a yellow base was seen in the center of the lesion. There was slight pallor of the disc. A similar lesion was seen in the left eye. Fields were normal. Physical examination and Wassermann test were negative. Red blood count was 3,500,000. Treatment included lextron ferrous capsules and vitamin B_1.

Case 4. This 26-year-old Negress was first seen on November 9, 1945, complaining of cloudy vision and pain in both eyes of two-weeks' duration. The first symptoms appeared when she was 17, at which time she was unable to see the blackboard

in school. At the age of 21, she was fitted with contact lenses.

There was a slight narrowing of the right palpebral fissure and mixed injection of the right bulbar conjunctiva. Both corneas were conical. An ectactic-leukomatous opacity about 4 mm. in size covered the papillary area, becoming more nebulous as it reached the limbus. Fine macular opacities were present, centrally and laterally, in the left cornea. The left fundus was seen merely as a red reflex. The right cornea stained with fluorescein; the left corneal epithelium was intact. The right anterior chamber was deep and, due to opacities, the fundus could not be made out. Refraction revealed a compound myopic astigmatism. Vision was: R.E. with a −4.00D. sph ⌒ −3.00D. cyl. ax. 165° = ability to see fingers; L.E. with a −3.50D. sph. ⌒ −3.25D. cyl. ax. = 0.1.

Diagnosis was: (1) bilateral conical cornea; (2) ectasia of the right cornea; (3) acute keratitis. Treatment consisted of pilocarpine solution, bichloride Hg ointment, and a tight bandage. This caused a recession of the cone to about 3 mm.; the mixed injection subsided; and the cornea improved.

In spite of the fact that the patient had worn contact glasses continuously eight hours a day for two years, the ectactic condition of the cornea was not alleviated and the degenerative processes continued.

Retinitis pigmentosa

Dr. Harold D. Bockoven presented two patients from Dr. Apple's service.

Case 1. A white man, aged 32 years, was first seen in August, 1945, complaining of marked loss of vision beginning at the age of 10. After examination at that time, he entered a school for the blind. Vision decreased progressively and, at the age of 21, he could no longer read. He has always been able to go about alone, having used a white cane for 10 years.

Family history showed that his father and mother were cousins. There were five children. An older brother was in a mental institution at the age of 13; the patient believed his brother's eyes were normal. Another older brother developed poor vision at the age of 10 and was totally blind at about 28 years of age. A younger brother had weak eyes and could no longer read at the age of 21. The sister's eyes were normal.

On examination, visual acuity, bilaterally, was light perception. Retinoscopy revealed refraction corrected by a + 3.00D. sph. ⌒ + 1.00D. cyl. ax. 90°, bilaterally. There were moderate vertical nystagmoid movements, more marked at the extremes of rotation. Pupils were 5 mm. in diameter and reacted poorly to light. There were discrete, sharply outlined, minute opacities situated in the anterior third of each lens, more marked on the left. These opacities were bluish when observed with the slitlamp.

The discs were pale and waxy in appearance, with indistinct edges. Both arteries and veins were moderately constricted. The fundi were tessellated, and there was a moderate amount of pigment of the bone-corpuscle type situated equatorially, frequently in close proximity to the retinal vessels. There was marked pigmentary disturbance at the left macula; both maculas appeared motheaten. Minute aneurysmal dilatations were present along the left superior temporal artery.

Case 2. A 50-year-old white man who was first seen October 17, 1945, complained of progressive loss of vision for five years, particularly in dim light. There was no history of past inflammation.

The patient had four brothers, two of whom had eye trouble; three sisters were normal. One brother, aged 46 years, had

had defective vision for 12 years, characterized early by night blindness, and was now practically blind. A second brother had a marked visual handicap, the nature of which is not known. There was no other significant family history, such as intermarriage.

Visual acuity equaled 0.1, bilaterally, and could not be corrected. Externally, a bilateral, diffuse, conjunctival injection and arcus senilis were noted. The pupils reacted to light and accommodation. The crystalline lenses were hazy bilaterally, posterior polar opacities being present. On fundus examination, the discs were pale and appeared waxy. The retinal vessels, particularly the arteries, were greatly attenuated. Both fundi were tessellated. Pigmentary deposits of a cobweb appearance were present equatorially. Bone-corpuscle type pigmentary deposits were present in both fundi, above and nasally. Some of these covered the blood vessels. Several large accumulations of pigment were situated peripherally. Bilaterally there was a peripheral form field, limited to from the 8- to the 10-o'clock positions, and a red field of 5 degrees.

Persistent tunica vasculosa lentis with fibrous hyperplasia

Dr. E. M. Green presented three cases from Dr. Apple's service.

Case 1. D. G., aged 29 months, was first seen at the age of five months and was one of twins born eight weeks prematurely. His weight at birth was 3 lbs., 12 oz. Two preceding pregnancies resulted in normal, full-term deliveries. The three siblings, including the twin, had had no ocular complaints and follow-up revealed no pathologic condition in the twin. There was no history of acute illness in the puerperium or in the patient postnatally.

Physical examination revealed no gross pathologic condition, excepting the ocular defects. Bilateral microphthalmos and a searching horizontal nystagmus were noted. Photophobia to strong light was present. An apparent dense, white corneal opacity occluded the iris on the right, temporally. The anterior chambers were shallow and the irides were light blue, with indistinct markings. With mydriatics, the right pupil dilated from 2 to 3 mm., irregularly and the left to 7 mm., evenly. On the Purkinje test, the light reflex from the posterior capsule of the lens was absent and, behind both lenses, was seen an opaque, white membrane on which blood-vessel remnants could be identified. A faint-red reflex was obtained from the nasal half of the left pupil. Tactile tension was normal.

The patient has been seen at regular intervals, and there has been no definite change in the eye findings.

Case 2. A. B., aged 11 months, was first seen at the age of five months with a history of increasing prominence of the right eye for the preceding two months. The patient was born 10 weeks prematurely and weighed 2 lbs. 13 oz. at birth. Otherwise, the history was of no significance.

Physical examination was negative except for the eyes. The left eye was microphthalmic. The right eye was enlarged, measuring 14 mm. in diameter. The left eye measured 10 mm. in diameter. The irides were light blue with indistinct markings, and the anterior chamber was absent or negligible, on the right, and shallow, on the left. The right eye was very firm on tactile tension, considerably more so than the left. Variable tonometric readings confirmed the tactile impression. An opaque, white membrane was noted behind the temporal portion of the right lens but, through the nasal portion, a clear view of a normal fundus and non-cupped disc was obtained. In the left eye, the membrane was more extensive, and only a faint-red reflex was obtained through the nasal half. Ciliary processes

extending in the left pupil were seen.

After a trephine of the right eye was performed on June 14, 1945, no further enlargement occurred. Normal ocular tension was obtained.

Case 3. P. P., aged two years, was first seen in October, 1945. She was born 10 weeks prematurely and weighed 1 lb. 13 oz. There was no history of acute illness during the puerperium or in the patient postnatally.

Physical examination was negative except for the eye findings and prominent frontal bosses. Photophobia to strong light was present. Both eyes were small and deep set, and a searching horizontal nystagmus was present. An apparent, whitish corneal opacity obscured the superior portion of the irides, bilaterally. The anterior chambers were extremely shallow or absent. The irides were light blue, the markings indistinct, and they had a fetal appearance. The pupils dilated irregularly, the right from 3 to 4 mm. and the left from 2 to 3 mm. with homatropine. The lens substance was clear, but the light reflex from the posterior lens capsule was absent. Behind both lenses was seen a thick, white, opaque membrane. There was no red reflex on either side. Laboratory and x-ray studies were not significant.

On October 10, 1945, a combined linear extraction of the right lens was performed, and an attempt was made to push the membrane to one side. Postoperatively, no iris coloboma was noted, and the small pupil present was occluded by fibrous adhesions. A wide complete iridectomy was performed on November 10, 1945. Nine days later, the findings showed the white membrane presenting anteriorly through a large pupillary opening.

Scientific program

Legal ophthalmology

Mr. Joseph Hinshaw read a paper on this subject which has been published in this Journal (September, 1946). Discussion was by Drs. Guibor, Soper, Hoffman, Mundt and Zeiss, and in closing by Mr. Hinshaw.

Robert Von der Heydt.

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THE 1946 ACADEMY MEETING

The week of October 13th to 18th, the Palmer House in Chicago unveiled one of the biggest and best conventions of the American Academy of Ophthalmology and Otolaryngology in its 51 years of existence. More than 3,000 members and guests registered, and every facility was bursting with more or less happy doctors in search of knowledge. The Academy meeting has often been likened to a three-ring circus, and the similarity continued in force this year, perhaps with a few more rings added.

The presence of many ex-medical officer members, old and new, resulted in impromptu reunions of veterans from the various theaters of operations, and many a hospital campaign was refought and experiences reviewed.

There were several innovations arranged for by the officers after much

thought and hard work. On the whole, these innovations were happy ones. The alternation of the Eye and Ear, Nose and Throat divisions in scientific assembly and instruction hours resulted in less crowding and more efficient handling, especially in the courses. The scientific programs were better than usual. The interspersing of motion pictures between scientific papers was an interesting experiment, meeting with favor by some and disfavor by others. In spite of some criticisms heard here and there, it would seem that most of the members enjoyed the new arrangement. The hall was crowded even through the last session.

The instruction courses were packed, and most of them were completely sold out. After the drought of the war years, everyone seemed thirsty for information and eagerly drank at the springs of knowledge set up in prosaic hotel rooms by the efficient secretaries.

The Jackson Memorial Lecture was given on the evening of October 16th by Dr. Alan C. Woods, the president-elect. The title of his comprehensive and stimulating address was "The influence of hypersensitivity on endogenous uveal disease." It is a valuable contribution to ophthalmology, summarizing what has been the author's life work of deep thought, study, and experimental research.

The Ear, Nose, and Throat members enjoyed an extra fillip in acting as hosts to the Pan-American Congress of Oto-rhino-laryngology and Broncho-esophagology which immediately followed the convention. The presence of outstanding South American scientists and particularly their vivacious and charming wives made the meeting a colorful one and added much to the gaiety of the gathering.

The scientific exhibits were well-chosen and displayed. This important feature of the Academy was always filled with members seeking what was new, and none left without adding something of great value to himself and to his patients. Ten of the 24 displays were from the ophthalmic division. Awards were given to Dr. Donald J. Lyle of Cincinnati, Ohio, for the teaching value of his extensive exhibit on "Neuro-ophthalmology;" to Dr. Walter H. Fink of Minneapolis, Minnesota, for the originality of his exhibit on "An anatomical study of the oblique muscles of the eye;" and to Dr. A. D. Ruedemann of Cleveland, Ohio, for the excellence of presentation of his exhibit on "Plastic eye implant." This last won the gold medal at the A.M.A. convention in San Francisco in June.

It was good to see so many familiar and friendly exhibitors displaying their goods and receiving orders in the Technical Exhibit Hall. Many of the orders will take a long time to be filled in these days of reconversion shortages, of course. But the display was there, with great promise of good things to come, and it was like old times. The war years had receded, and one was back again, seeing, handling, comparing, and discussing the tools of his trade with his colleague and exhibitor just as if a cataclysm had not occurred.

At the luncheon given to the faculty by the president, Gordon B. New, the Leslie Dana Medal of the National Society for the Prevention of Blindness, the St. Louis Society for the Prevention of Blindness, and the Association for Research in Ophthalmology was presented to Harry S. Gradle for his outstanding contributions to the prevention of blindness, to ophthalmology, and to the teaching of ophthalmology. Conrad Berens gave the presentation citation which will be printed in the Journal in a subsequent issue, and the medal to Mrs. Gradle representing her husband who was prevented by illness from being present, much to our regret and sorrow, for Harry Gradle is one of our best loved members.

In spite of its size, which is increasing yearly, the Academy functions on well-oiled and well-guided ball bearings. One need have no misgivings as to its future, for it is here to stay in very much its present form for many years to come, because it gives utmost service to each of its eager and loyal members.

Derrick Vail.

TRAINING NONMEDICAL HELPERS IN OPHTHALMOLOGY

As to possibilities of development for the good of ophthalmology, and therefore of the general public, perhaps the most important paper presented to the recent San Francisco meeting of the American Ophthalmological Society was that read by Parker Heath on "Medical Assistance at Professional Level."

Heath recognizes a serious shortage of physicians, not only as existing at the present time, but as likely to continue for some years to come. The war has had much to do with causing this shortage which is especially serious in the field of ophthalmology; but some of us may be disposed to question whether the shortage is more particularly one of personnel or rather of effective training of that personnel.

The remedies so far proposed include "larger classes at undergraduate level, increasing the number of residents and internes, provision for more fellowships, refresher courses, and basic training programs in the specialties."

The medical profession, we are reminded, has trained special groups of lay persons to aid in caring for the sick. These groups include nurses, laboratory helpers, X-ray technicians, office employees, and special workers in research. The only department in which ophthalmology has made a serious attempt to cope with the problem of training expert assistants is that of orthoptics.

Heath suggests that ophthalmology is probably more adaptable to professional assistance than any other specialty. Aspects of ophthalmology suggested as lending themselves to special training and utilization of lay assistants include refraction, muscle balance, tonometry, external and ophthalmoscopic examination, photography, some forms of therapy, perimetry, screening tests in schools and industry, the care and preparation of instruments, assistance during operations, laboratory procedures, the fitting of contact glasses, and the assembling of material for scientific essays.

It is apparently contemplated that nonmedical persons, expertly trained for these multifarious activities, shall assume much of the work at present undertaken by medical graduates who either have received a more or less complete training in ophthalmology or are seeking such training under the preceptorship of the medical chief with whom they are associated.

It is pointed out that at the present time many of us delegate parts of our examination of patients to personnel trained by the preceptor method, "a method which requires many years and does not turn out enough well-rounded trained people to meet the demands or the possibilities." To increase the numbers of such persons, and to insure their proper training, Heath would establish a special college curriculum of four years and leading to a bachelor's degree. The first two years of such a course would be taught by the usual literary and scientific faculties, while the last two years would be devoted to the medical field, and responsibility for them would devolve upon medical teachers. The author's outline of a curriculum for these last two years includes most of the subjects ordinarily taught to graduate students in ophthalmology. For example, it is proposed to devote 240 hours to anatomy including

dissection, 576 hours to refraction, 216 hours to physiologic chemistry, 144 hours to histology of the eye, 216 hours to pathology, 144 hours to clinical and laboratory technique, 72 hours to ocular muscles, 280 hours to orthoptics, and 200 hours to perimetry.

It may be assumed that this proposal to create an important new professional group has grown out of the urgent need of those who are carrying on large ophthalmic practices, as well as in many instances administering important public clinics. Such leaders in ophthalmology have no doubt tried and found wanting the usual employment of medical assistants or associates, as well as the rather slow and laborious process of preceptorship as applied to a well-educated secretary or nurse. Many medical assistants and associates have been grievously missed during the war period. Some of them have returned from war service anxious to carve independent careers.

To many of us, sympathetic consideration of the present proposal may suggest questions as to its effect in the first place upon the individual ophthalmologist who might employ the new type of graduate, and in the second place upon the practice of ophthalmology as a whole.

How long, we may inquire, would it take not merely to induce a number of important colleges to create such a course leading to a degree, but also to interest a large body of students in such a course? At first the applicants are likely to be drawn from the ranks of those high school students or graduates who have already felt themselves impelled toward the regular nurse's training. Further, how long would it take to induce a large number of ophthalmologists to replace their present helpers by such new graduates?

Allowing for the time necessary to attract a body of students, for the length of time to be occupied by the course itself, and for the education of the profession of ophthalmology in the utilization of such graduates, it seems not unlikely that ten or twelve years would be a moderate estimate of the period within which we could expect a large number of such nonmedical graduates to have been launched upon their new career.

To what extent would the provision of such highly trained nonmedical office assistants tend to reduce the opportunities for development of young ophthalmologists who might expect to start their careers as assistants to established practitioners of the specialty? Is the desire to establish such a nonmedical graduate group partly based upon the fact that medically qualified assistants have ambition beyond that which may be expected of a lay assistant, and are apt sooner or later to undertake their own competitive practice of ophthalmology?

Is it to the advantage of the general public that much of the practice of ophthalmology shall be concentrated in the hands of a few leaders who make use of lay assistants, or will such public advantage be best served by the training of as many medical ophthalmologists as the market can support?

Is there not much to be said in favor of the individual and direct personal relation between ophthalmologist and patient rather than the delegation of professional tasks to a lay assistant who reports back to the ophthalmologist?

Would not the length of time necessary to produce substantially useful results from the new proposal be better utilized in working toward the creation of improved facilities for the postgraduate training of medical men in ophthalmology?

Many leading ophthalmologists are at present excessively overburdened with the teaching of undergraduate and postgraduate medical students. Really intensive

training of those preparing for expert assistantship to ophthalmologists might be expected to add materially to the educational labors of those called upon to establish such facilities. If the training bestowed upon this new group of students is not of the highest possible quality, it is not worth giving at all.

Too many physicians practicing eye, ear, nose, and throat in the larger country towns are appreciably better trained in otolaryngology than in ophthalmology. Such men might easily delegate a large part of their work in ophthalmology, and especially in refraction, to a graduate lay assistant, who then might easily prove to be the rather effective competitor of an independent ophthalmologist in the same town. Such a contingency could hardly be regarded as generally advantageous to ophthalmology as a whole.

Is there any possibility that a considerable number of these specially trained lay assistants would be enticed into selling their services to osteopaths or chiropractors, or even to optical concerns which advertise expert examination in refraction?

Have not the older ophthalmologists, firmly established in their specialty, a moral duty to assist in the development of a younger generation of medical ophthalmologists rather than in the creation of a new nonmedical group of workers in the specialty and particularly in the practice of refraction?

In its ultimate elaboration, the proposed scheme for training of expert office assistants below the graduate medical level might prove of great public benefit, especially in the event of development of a large measure of socialization of medicine. Whether it would be of general advantage to the profession of ophthalmology, as at present constituted, is a question to which we may properly devote serious and deliberate consideration, bearing in mind every conceivable aspect of the subject.

W. H. Crisp.

DI-ISOPROPYL FLUOROPHOSPHATE IN GLAUCOMA

During the past few years several new drugs have been introduced for the treatment of glaucoma. The most recent of these is Di-isopropyl Fluorophosphate (D.F.P.). The fluorophosphates have been shown to be powerful parasympathamimitic drugs due to their ability to destroy cholinesterase. They are quite toxic and during the recent war were considered as potential chemical warfare agents by both the enemy and ourselves. In the course of chemical warfare experiments, the marked miotic effect of D.F.P. on the pupil suggested its possible use in the treatment of glaucoma.

D.F.P. [$(C_3H_7O_2)_2$ P O F] is a rather unstable compound with a faint fruity odor. Its freezing point is $-50°$C., and its boiling point is 183°C. Its stability is greatly enhanced in solutions of peanut oil.

The recently published clinical investigations of McDonald and of Leopold and Comroe indicate that we have in D.F.P. a valuable addition to the arsenal of antiglaucomatous agents. In many cases, it will control the intraocular pressure when the more conventional treatment with eserine and pilocarpine has failed. In others, it will be no more effective than these standard drugs have been. Its chief advantage seems to be in its prolonged action, and the lack of necessity for frequent instillations. Another valuable asset is its ability to overcome the mydriatic and cycloplegic effect of atropine. This will be welcome news to those ophthalmologists who have had the misfortune to deal with a case of glaucoma precipitated by cycloplegic examination, or by

the mistaken use of atropine for a miotic.

Like any other miotic D.F.P. may produce certain untoward affects. It can cause ocular and brow pain due to powerful ciliary spasm. Headache and photophobia have been complained of following its use. Systemic affects from absorption from the conjunctival sac have occurred in experimental animals; one drop of the full-strength solution in the eye of a rabbit has caused death within two to three minutes. Therefore, it is a drug to be treated with respect and not used indiscriminately. However, Leopold and Comroe have not found any systemic affects in man when employing it in 0.2-percent solution, an observation which agrees with this writer's experience.

Other series of cases must be studied before D.F.P. becomes available for general use. Time will tell whether or not it will prove as effective as preliminary reports make it appear to be.

Edwin B. Dunphy.

BOOK REVIEWS

OPHTHALMOLOGY IN THE WAR YEARS. Vol. 1 (1940-1943). Edited by Meyer Wiener, M.D. Clothbound, 1,166 pages, references, subject index, and author's index. Chicago, 304 South Dearborn Street, Year Book Publishers, Inc., 1946. Price, $13.50 postpaid.

Thirty-six contributors, most of whom are widely known and all of whom are experts, combined under the able editorship of Dr. Wiener to produce a volume of great practical use and value to all English-reading ophthalmologists. The cruel war years, among other and less serious things, forced many ophthalmologists either through isolation in military service or through the overburden of routine office work, to give up the reading of current ophthalmic literature, which is the life blood of progress in our great specialty. To fill in this gap in our knowledge, the present volume and its subsequent fellow were conceived.

The editor says in his preface that "it has been the purpose of the editorial staff to supply as complete a bibliography as possible and to give not merely an abstract but a running comment on articles which, in each editor's estimation, merited a review." These purposes have been amply fulfilled, to the great credit of the contributors and the staff. When one considers how busy these men and women were and are, what difficulties were encountered in obtaining the articles, the restricted lists of foreign journals and ophthalmic literature in general, and other hardships in war-time, one can but marvel that such a splendid and complete piece of work could result.

Each contributor read, digested, reviewed, and commented on anywhere from 50 to 800 published articles in his particular field. The expert judgment shown in discrimination makes each chapter an authority of the subject under discussion, and emphasizes the peaks of progress in our specialty in the years January, 1940, through December, 1943.

All parts of ophthalmology are covered, including, as well, comparative ophthalmology, hygiene, sociology, education and history, methods of examination, and industrial ophthalmology.

One is indeed proud of this achievement in American ophthalmology, and grateful for the wealth of ophthalmic literature, collected under such trying conditions, that is made available in one volume to all of us. That it will be fruitful and productive of ideas, useful in the solution of one's daily problems, and a ready source of reference and stimulation needs no comment. The editor, the contributors,

and the publishers are to be congratulated, commended, and thanked by ophthalmologists everywhere.

Derrick Vail.

DISEASES OF THE EYE. (Revised edition.) By Konstantin Pascheff. 495 pages, 288 illustrations, 12 plates. Sofia, University Publication, 1946.

This is the second edition of the first textbook on ophthalmology in the Bulgarian language, and it is supplemented by the ophthalmic advances made from 1929 to 1946. The author is a prolific contributor to ophthalmic literature, and he uses much of his published material in this book. The book is divided into 12 chapters, dealing with diseases of the orbit, lids, lacrimal apparatus, motor system, sensory and sympathetic systems, conjunctiva, cornea-sclera, uvea, visual apparatus, the lens and vitreous, and the globe including glaucoma and anomalies of refraction. The last chapter deals with surgery as it is being performed in the author's clinic at the University of Sofia. Each chapter covers briefly methods of examination, congenital anomalies, circulatory disturbances, inflammation, degeneration, injury, tumor, prophylaxis, and therapy. The profuse illustrations with drawings, photographs, and microphotographs, and the condensed, although precise and clear, descriptive material will widen the ophthalmic horizon of the medical student without burdening him with much reading. The textbook is, nevertheless, sufficiently complete to be of value to the general practitioner and to serve as an excellent guide to the student of ophthalmology. Worthy of note are the plates of illustrations on trachoma and congenital ectopia of the lens.

Ray K. Daily.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below, which broadly correspond to those formerly used in the Ophthalmic Year Book. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. General methods of diagnosis
2. Therapeutics and operations
3. Physiologic optics, refraction, and color vision
4. Ocular movements
5. Conjunctiva
6. Cornea and sclera
7. Uveal tract, sympathetic disease, and aqueous humor
8. Glaucoma and ocular tension
9. Crystalline lens
10. Retina and vitreous
11. Optic nerve and toxic amblyopias
12. Visual tracts and centers
13. Eyeball and orbit
14. Eyelids and lacrimal apparatus
15. Tumors
16. Injuries
17. Systemic diseases and parasites
18. Hygiene, sociology, education, and history
19. Anatomy, embryology, and comparative ophthalmology

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VISUAL TRACTS AND CENTERS

Damel, C. S., Dickmann, H. G., and Just Tiscornia, B. **Considerations on five cases of optochiasmic leptomeningitis.** Arch. de Oft. de Buenos Aires, 1943, v. 18, Oct., p. 481.

The authors, who prefer the term optochiasmic leptomeningitis to the more common one of optochiasmic arachnoiditis, report their findings in five cases of this disease, in all of which the clinical diagnosis was verified at operation. The greater incidence of the condition in men in the second and third decades of life is stressed. The disease may be primary and the chiasm involved alone, or it may be secondary to other diseases affecting the central nervous system, such as encephalitis, tabes, and multiple sclerosis. The etiology is quite varied; trauma, focal infection, tuberculosis, and syphilis are the most common causes. While polymorphism of the visual fields is characteristic of the disease, concentric and irregular contraction is the most frequent perimetric occurrence. The fundus generally shows optic atrophy, although this may exceptionally be accompanied by edema. The authors favor early surgical intervention, not only in cases of known etiology, in which the medical treatment fails to arrest the progress of the disease, but also in those cases in which the etiology is unknown. They believe that a judicious combination of medical and surgical treatment will improve the percentage of favorable results. (Visual fields, tables, and bibliography.)

Plinio Montalván.

Godtfredsen, Erik. **Ophthalmologic and neurologic symptoms of malignant nasopharyngeal tumors.** Acta Ophth., 1944, Supplement 22, pp. 273. (See Section 15, Tumors.)

Hughes, E. B. C. **Some observations on the visual fields in hydrocephalus.** J. Neurol. Neurosurg., and Psychiat., 1946, v. 9, Jan., pp. 30-39.

Little attention has been paid to chiasmal changes produced by a dis-

tended third ventricle in obstructive hydrocephalus. There has been some confusion because of papilledema and secondary optic atrophy. The patients studied in this series are without evidence of optic atrophy. The earliest change is very small paracentral scotomas in the apex of the lower temporal quadrant which is usually bilateral. The scotomas are thin, have small visual angles, and are usually centrocaecal. As the scotoma gradually enlarges the adjacent isopters become involved locally. The next change is a depression of visual acuity in the affected quadrant and is characterized by a recession of the central isopters and graying of the affected fields (white objects appear hazy, dirty, gray, pale green). Graying is seen more commonly in chiasmal lesions, and stops at the midline inasmuch as crossed fibers are involved. With further progress the depression type of field comes into play and a gradual loss of central isopters ensues until most of the lower temporal quadrant is lost. Later some graying occurs in the nasal field. Small scotomas may also appear in the upper temporal quadrant. I. E. Gaynon.

Porsaa, Kaj. **The central visual field after occipital lobectomy.** Acta Ophth., 1944, v. 22, pt. 2, pp. 243-260.

Porsaa reviews the literature on bilateral representation of the macula, and reports five cases of hemianopsia without sparing of macular vision after occipital lobectomy for neoplasm. In one case, there was macular sparing preoperatively, but it was lost after the operation. Porsaa believes that these observations conclusively prove the absence of bilateral cortical macular representation. The sparing of the macula, when it is found, is to be attributed to an extensive macular representation in the calcarine area, part of which is left intact. Ray K. Daily.

Traquair, H. M. **The nerve fibre bundle defect.** Trans. Ophth. Soc. United Kingdom, 1944, v. 64, p. 3. (See Section 10, retina and vitreous.)

Zeligs, M. A. and Joseph, G. F. **Unilateral internal ophthalmoplegia.** Arch. Neurol. and Psychiat., 1945, v. 54, Nov.-Dec., p. 389.

Isolated unilateral ophthalmoplegia may be the only clinical sign in a patient with syphilitic meningitis. A case history illustrating such an occurrence is presented. The diagnostic importance of serologic study in cases of unexplained pupillary paralysis is emphasized. The rapid therapeutic response to penicillin therapy is mentioned. The probable anatomic site of such a lesion is postulated. Theodore M. Shapira

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EYEBALL AND ORBIT

Bardram, M. T. **Progressive exophthalmos (so called malignant exophthalmos).** Acta Ophth., 1944, v. 22, pt. 1, pp. 1-26.

The literature of exophthalmic ophthalmoplegia is reviewed, and three cases following thyroidectomy are reported. All three cases had an increased output of gonadotropic hormone, and one had an increased metabolic rate with other symptoms of thyrotoxicosis. In one patient the exophthalmos abated after a Naffziger decompression; in the other two it was controlled by conservative treatment. (3 illustrations.)
Ray K. Daily.

Bengisu, N. **A crouzon type of craniofacial dystosis in a father and daughter.** Oto-Nöro-Oft., 1946, v. 1, pp. 1-5.

The author reports two cases of cranio-facial dystosis characterized by the triad of exophthalmus, and deformity of the cranio-facial and maxillary bones. The anterior segment of the father's eyeball had been amputated because of lagophthalmic keratitis. The daughter had an early postedematous optic atrophy. I. E. Gaynon.

Bertotto, E. V. **Congenital paralysis of the lateral rectus and melanosis bulbi.** Anales Argentinos de Oft., 1945, v. 6, Apr.-May-June, pp. 60-62. (See section 4, Cornea and Sclera.)

Blegvad, Olaf. **Myxoma of the orbit.** Acta Ophth., 1944, v. 22, pt. 2, pp. 131-140.

The five cases reported in the literature are briefly reviewed and an additional one is described clinically and histologically. In the course of six years a woman, 29 years of age, developed a hyperopia of eight diopters in the left eye and a tumor the size of a walnut in the temporal side of the left orbit. The symptoms, in addition to the refractive changes were exophthalmos, impaired ocular motility, loss of vision, pain in the eye, and a stellate folding of the retina, with the macula as a center. The retina in this area was edematous, and the author attributes the folding to pressure by the tumor. Five months after the surgical removal of the neoplasm the exophthalmos subsided, the ocular motility was restored, but the retinal folding, impaired visual acuity, and hypermetropia were still present. (4 illustrations.)

Ray K. Daily.

Erpf, S. F. Wirtz, M. S. and Dietz, V. H. **Plastic artificial eye program, U.S. Army.** Amer. Jour. Ophth., 1946, v. 29, August, pp. 984-992. (8 figures, references.)

Cutler, N. L. **A basket type implant for use after enucleation.** Arch. of Ophth., 1946, v. 35, Feb., pp. 71-83.

The author describes a new type of orbital implant which has been used 50 times in an Army general hospital. Following enucleation, a specially constructed basket-like implant is secured in Tenon's capsule by three sutures. The sutures are tied over a button which is forced down into the implant in such a way as to produce a depression in the socket. Both implant and button are made of Lucite (methyl methacrylate). A plastic retainer is then placed behind the lids and a moderate pressure bandage is applied. Within three weeks a special plastic artificial eye may be worn.

Actual measurements of motion were made on 20 patients in which there had been no implant, 20 with a ball implant, and 20 with the new basket implant. The average range of motion expressed in degrees for no implant was 69, for the ball implant 74, and for the basket implant 109. It was found that with the basket implant and a new type of prothesis there was more instantaneous movement and a wider range of action. Thirteen illustrations depict the operative technique. John C. Long.

García Nocito, P. F., and Zubillaga, J. B. **Frost-Lang operation.** Arch. de Oft. de Buenos Aires, 1943, v. 18, Oct., p. 513.

After discussing the different techniques for enucleation with implant, the authors express their preference for the Frost-Lang operation. They used vitallium and lucite implants with very good results. The article is illustrated. Plinio Montalván.

Givner, Isadore. **Reconstruction of the floor of the orbit.** Amer. Jour.

Ophth., 1946, v. 29, August, pp. 1010-1012. (3 figures, references.)

Godtfredsen, Erik. **Orbital complications following operations on the paranasal sinuses.** Acta Ophth., 1944, v. 22, pt. 4, pp. 401-418.

The conclusions are reached from a study of 42 cases gathered from the literature and eight cases in the author's personal experience. The tabulated data show that in surgery of the frontal and maxillary sinuses orbital complications are rare and insignificant. They are more frequent and severe after surgery of the ethmoid labyrinth, usually in the form of orbital hematoma or optic nerve lesions. At the onset of orbital complications the eyegrounds should be examined; the appearance of orbital stasis is an indication for orbitotomy and orbital drainage, which if performed promptly will restore vision. Unless this is done within 24 hours of the onset of an optic nerve lesion the prognosis is poor. (4 illustrations.) Ray K. Daily.

Ingalls, R. G. **Penetrating wounds of the cornea with hypopyon treated with penicillin.** Amer. Jour. Ophth., 1946, v. 29, Sept., pp. 1152-1154. (2 figures.)

Jaquelin, A., Turiaf, J. D. **Atypical ocular tuberculosis; tuberculin tests; and tuberculin therapy.** Ann. d'Ocul., 1945, v. 178, Nov., pp. 514-527.

Atypical tuberculous lesions are relatively frequent not only in the eye but also in the joints, skin, bronchi, and nervous system. The injection of tuberculin in sufficient amount will produce aggravation of usually mild chronic lesions in these parts if they are tuberculotoxic in origin. Their frequent association leads the authors to consider them as a syndrome, characterized by pathologic lesions found in tuberculosis but without the presence of the specific organism. The subcutaneous injection of tuberculin is advised for diagnosis and treatment. For diagnostic purposes, 0.5 mg. is injected subcutaneously. If no reaction occurs in four days 1 mg. is given, and if necessary 5 mg. is injected four days later. In treatment with tuberculin one strives to avoid a general or local reaction. Of 48 patients, 26 were considered cured, that is the process was inactive for more than two years There were 13 cases of iridocyclitis, 6 of iritis, 3 of sclerokeratitis, 2 of keratoconjunctivites, 1 of iridochoroiditis, 1 of uveitis. Among the complete failures were 3 cases of iridocyclitis, 2 of sclerokeratitis, 1 of iritis, 1 of iridochoroiditis, 1 of chorioretinitis, and 1 of choroiditis. In thousands of injections only two fatalities could possibly be attributed to tuberculin injections. In a man, 63 years of age, fatal meningitis occurred shortly after the injections were begun. In another patient, severe hemoptysis followed the injection of tuberculin.

Chas. A. Bahn.

Jensen, C. F. D. **Tantalum enucleation implant.** Amer. Jour. Ophth., 1946, v. 29, Sept., pp. 1151-1152. (3 figures, references.)

King, E. F., and Samuel, E. **Fractures of the orbit.** Trans. Ophth. Soc. U. Kingdom, 1944, v. 64, pp. 134-154.

The authors present the classification of fractures of the face of McIndoe and describe several types of fractures of the nasomaxillary complex or central bony mass. In an upper fracture the line traverses the root of the nose and in the orbit divides the roof from the inner and outer walls. The facial bones are separated from the cranium and

severe intracranial hemorrhage ensues. In a middle fracture the line traverses the nasal bones, the inner wall and floor of orbit to the infraorbital foramen, and the anterior face of the maxilla to the pterygo-mandibular fossa. The detached bony mass tends to be displaced backwards and a flattened dishface results.

Another type of fracture which is not frequent is a downward displacement of part of the orbital floor, unassociated with any damage to the margin of the orbit or surrounding facial bones.

Damage to the eye must be given first place in diagnosis and treatment. Hemorrhage that appears in the lids some hours after an injury suggests an underlying fracture. Surgical emphysema indicates communication with the ethmoid cells or antrum. It increases on blowing the nose and usually subsides in a few hours. Loss of continuity of the orbital margin with local tenderness indicates an orbital fracture. Proptosis is due to displacement of the globe by bony fragments or hemorrhage within the cone of muscles. When it occurs some weeks or months later it indicates an arteriovenous aneurysm, usually of the cavernous sinus and occasionally of the orbital vessels. It is accompanied by a bruit, pulsation of the globe, and congestion of the veins of the lids and retina. Proptosis may lead to exposure keratitis. Endophthalmos and downward displacement of the globe can be due to depression of the orbital floor if there is an associated rupture of the suspensory ligament of Lockwood. An intractable sinus may result from a foreign body. Anesthesia in the areas of distribution of the infraorbital or other branches of the trigeminal nerve also suggests fracture. Traumatic stricture of the nasolacrymal duct with secondary infection of the sac may occur in fractures of the nasomaxillary complex.

Pressure on the nerve in the optic canal, hemorrhages into the nerve sheath, traumatic arachnoiditis, and lesions of the vessels that supply the optic nerve result in reduction of vision. Diplopia is the most important ophthalmic sequel and is often the dominating permanent disability.

In the early stages treatment consists of reduction of the bony deformities. Later little more than cosmetic improvement by the insertion of subcutaneous bone-grafts is possible. The defective movement of the globe usually can be corrected surgically only if it is due to paralysis of individual muscles. (12 figures.)

Beulah Cushman.

Lech Junior. **Plastic operations on the orbital cavity.** Arquivos do Instituto Penido Burnier, 1945, v. 7, Dec., pp. 30-56.

The paper deals with correction of the orbital cavity for readaptation of prothesis. The subject is covered under the headings of bloodless dilatation, topographic anomalies, absence of lower cul-de-sac, subtotal and total retractions of the cavity, and conclusion. The methods of a number of authors are described and illustrated. (23 illustrations, bibliography.)

W. H. Crisp.

Mata Lopez, Pedro. **Concerning a form of ocular sympathalgia.** Arch. de la Soc. Oft. Hisp.-Amer., 1945, v. 5, May, pp. 371-377.

There are certain patients who complain of dull pain about the orbits that is sometimes associated with close work but not dependent upon it, vaso-

motor disturbances of the anterior pole of the eye of the sympathetic type, slight photophobia, and at times slight rhinorrhea. The syndrome seems to have features in common with the syndrome of Sluder and possibly should be included with it. Phenolization of the spheno-palatine ganglion has been found to produce a rapid and lasting cure. J. Wesley McKinley.

Moras, P. V., Deschamps, J. L., and Ardouin, M. **Diagnostic remarks and therapeutics of ocular tuberculosis.** Ann. d'Ocul., 1945, v. 178, Nov., pp. 490-513.

In a detailed study of 30 patients, 10 were male, 20 female, and more than half under 25 years of age. In one half of the patients only one eye was affected. The following conditions other than simple phlyctenulosis, were observed: kerato-conjunctivitis, recurrent phlyctenular type, 2; interstitial keratitis, nodular type, 1; sclerakeratitis, 7; iritis and iridocyclitis (anterior uveitis) 10; hyalitis and diffuse choroiditis (posterior uveitis) 6; circumscribed choroiditis 2; tuberculous periphlebitis 1; recurrent hemorrhage 1. In several patients the following sequence was noted: phylctenulosis, sclerokeratitis, iritis, anterior uveitis, and posterior uveitis. In the thirty patients studied not one case of classical ocular tuberculosis was observed. Twenty-five percent of the patients had tuberculous antecedents. A positive cutaneous tuberculin reaction was considered of value only in the very young. Radiologic examination of the thorax, done in every patient, frequently did not show active lesions concurrent with the ocular lesions, but did show scars and calcification. Among the clinical manifestations observed were recurrences after fatigue and healing after rest and other hygienic measures. Scleral involvement in phlyctenular recurrences, slight corneal vascularization, a chalky appearance of the cornea, segmentary or annular corneal lesions were frequently observed. In iridocyclitis common manifestations were hemorrhage into the iris, large gray adherent fibrinous exudates, and early depigmentation of the iris. Secondary glaucoma occurred in three of ten eyes with uveitis. Tuberculous iridocyclitis may develop rapidly after a sudden onset and may improve after injections of mercury cyanide. In choroiditis changes of pigmentation are slight, delayed, and limited to the margins of the lesion. Of little value were the Verne resorcin reaction, globular sedimentation, and the Besredka complement reaction. The tuberculin test is considered final, quantitatively and qualitatively. One, two or three subcutaneous injections of tuberculin are used depending on the amount and character of the reaction. The first injection consists of 1 cc. of a solution containing 1 mg. of tuberculin. If negative, in three days a second injection of 3 mg. in similar dilution is administered and in five days 5 mg. is injected. The reactions may be local, general, or ocular. The last consists of increased sensitiveness, photophobia, slight diminution of vision, increased injection, increased hemorrhage, and hypertension. If intelligently used, permanent ill effects are rare. A positive reaction is definitely diagnostic of a tuberculous etiology and a negative reaction rules it out with equal certainty. The treatment advised is tuberculin in small but increasing doses with avoidance of a focal or general reaction. Six months may be required for appreciable im-

provement and twelve months for a cure. Tuberculin treatment is contraindicated in advanced or hemorrhagic pulmonary tuberculosis. Residence in altitudes more than 5000 feet above sea level is considered an important adjunct to other treatment. Among auxiliary treatments considered worthy of further study are local light therapy, autohemotherapy, and the prolonged injection of vitamin D and calcium. A detailed analysis of the progress and treatment of the 30 patients studied is reported. Chas. A. Bahn.

Quintana, Juan. **Orbital mixoma.** Arch. de la Soc. Oft. Hisp.-Amer., 1945, v. 5, May, pp. 346-351.

A pure orbital mixoma is rare. Such a tumor was found in the anterior inferotemporal position of the orbit. It caused exophthalmos with displacement of the globe upward and inward. Extirpation was complete without recurrence in six months.

J. Wesley McKinley.

Rønne, Gerhard. **Local treatment of intrabulbar infections. The clinical and histological picture of staphylococcus infection.** Acta Ophth., 1944, v. 22, pt. 1, pp. 105-116.

A clinical and histological description of the course of experimental intrabulbar staphylococcus infection, into the anterior chamber, and into the vitreous is presented. Fifty bacteria of the strain used by the author injected into the vitreous were sufficient to produce perforation of the eyeball within four days. The symptoms, which appeared on the second day, were exophthalmos, corneal edema, and conjunctival injection and secretion. The histological picture is characterized by a primary reaction in the retina and ciliary body; choroidal changes appear later, and the anterior ocular segment remains free of bacteria for a long time. Ray K. Daily.

Rudemann, A. D. **Plastic eye implant.** Amer. Jour. Ophth., 1946, v. 29, August, pp. 947-952. (11 figures.)

Rundle, F. F. **Observations on a case of orbital varix.** Clinical Science, 1945, v. 5, Dec., pp. 139-144.

This condition produces a characteristic clinical syndrome including the dramatic phenomenon of transient severe proptosis. A man, 45 years of age, complained of a protrusion of his right eye on stooping. The position of the right eye in its orbit varied in the different positions of the body whereas the left eye remained in the same position at all times. The Hertel exophthalmometer was used for measurements. When the cervical veins were compressed by means of a pneumatic cuff placed around the neck, the exophthalmos reached a maximum of 18 mm. At this point the eyeball moved 2 mm. laterally but not upwards or downwards. Recession proceeded rapidly after release of the compression. The visual acuity and field, fundus, pupil, and pupillary reactions were normal. When maximal compression was maintained for five to eight seconds the eye became blind, but vision returned to normal ten seconds after compression was released. Distinct pulsation of the globe, synchronous with the carotid pulse, occurred when the bulb was fully protuded.

Francis M. Crage.

Rundle, F. F., and Wilson, C. W. **Development and course of exophthalmos and ophthalmoplegia in Graves'**

disease with special reference to the effect of thyroidectomy. Clinical Science, 1945, v. 5, Dec., pp. 177-194.

Measurements provide no support for the claim that exophthalmos may develop abruptly, even over night, and that it may vary greatly from day to day. Widening of the palpebral fissure from lid retraction may at times be rapid and create the illusion of increased exophthalmos. Measurements of ocular prominence were made with Hertel's exophthalmometer, modified by the inclusion of a central stop to give greater accuracy The vertometer measured the range of elevation.

Stages of ingravescence and remission occur in the course of exophthalmos and related eye signs in Graves' disease. The former is called the dynamic and the latter the static phase. The dynamic precedes the static phase.

The exophthalmos develops at the rate of 0.5 mm. per month with a concomitant development of paralysis of elevation. The latter loses four to five degrees for each millimeter of protrusion. Exophthalmos and ophthalmoplegia are slower and less complete in their progressive stage.

The position of the globe depends on the volume of the orbital tissues. The orbital change is a true growth of tissue and the resultant exophthalmos, as indicated by the curves is of the same order in all cases, even after thyroidectomy. The increased exophthalmos after thydoidectomy is not due to excess thyroid hormone. It is merely evidence that the patient was probably in the dynamic phase of the disease. The orbital tissue growth seems to be produced by some nonthyroid hormone. After thyroidectomy for thyrotoxicosis, the exophthalmos and range of elevation of the eye showed little change. When a slight increase in protrusion occurred it could be ascribed to recovery from loss of weight.

Francis M. Crage.

Sugar, S. H. and Forestner, H. J. **Methacrylic resin implant for sunken upper lid following enucleation.** Amer. Jour. Ophth., 1946, v. 29, August, pp. 993-1000. (6 figures, references.)

Toni, S. S. **A case of anophthalmos.** Manitoba M. Rev., 1946, v. 26, Feb., p. 73.

The author briefly relates the history of this developmental anomaly and presents his own case in which a bilateral anophthalmos was present in an otherwise normal child.

Francis M. Crage.

Wheeler, Maynard. **Exophthalmos caused by eosinophilic granuloma of bone.** Amer. Jour. Ophth., 1946, v. 29, August, pp. 980-983. (2 figures, bibliography.)

Wolff, Eugene. **Hyaline bodies in the intraocular fluids and tissues.** Trans. Ophth. Soc. U. Kingdom, 1944, v. 64, p. 179.

The author describes hyaline-like bodies that are found in the intraocular fluids and tissues and are derived from the blood. Some called hemoglobin bodies, stain bright pink with eosin and are usually formed by a clumping together of about 25 red cells. They occur in the aqueous and vitreous in acute and subacute inflammations associated with hemorrhage. They are not nucleated but may engulf a cell, a nucleus, or any solid matter such as pigment.

Fibrin bodies typically are rounded bodies. They may be much smaller than a red cell or four to five times as

large. They may not be strictly circular but their margin is not as irregular as that of a hemoglobin body. The bodies may settle on the internal limiting membrane and become hemispherical. In early stages they stain pink, as they grow older they take on the blue (basophilic) stain and eventually they may become calcified. They may be surrounded by cells. They are more often seen in acute and subacute inflammations than in chronic.

The author distinguishes both types from Russell bodies which are hyaline spherules formed in chornic inflammatory conditions only in the presence of plasma cells. In the eye they are found in the iris, ciliary body, choroid, retina, and conjunctiva. Beulah Cushman.

Woods, A. C. **The ocular changes of primary diffuse toxic goiter.** Medicine, 1946, v. 25, May, pp. 113-154.

This comprehensive review discusses, in great detail, the usually noted ocular changes of primary toxic goiter. In the first section, all of the lid signs are described, and the author explains each one, in terms of the relationships between relaxation of the orbicularis muscle, overaction of the levator muscle and increased tone of the palpebral smooth musculature. The last mentioned factor is a logical one, in view of other evidences of sympathicotonia in toxic goiter.

Under the heading of external ocular changes, the author discusses weakness of convergence (Moebius' sign), abnormal pigmentation of the skin of the lids (Jellinek's sign), adrenalin-sensitized pupils (Loewi's sign), and excessive lacrimation.

Two types of patients with extraocular muscle palsies are described. The patients in the first group have isolated or multiple pareses, with no definite pattern of involvement. These occur with exophthalmos, and disappear when the thyrotoxicosis is controlled. Organic changes analogous to those of myasthenia gravis are sometimes found in these muscles. However, there is no favorable response to prostigmine. In the other type ocular-muscle palsies occur in "malignant exophthalmos," or "exophthalmic ophthalmoplegia." The muscle changes progress even after thyroidectomy. The muscles show hypertrophic myositis, fibrosis and edema. This condition has been related to postoperative changes in pituitary function, and treatment must include thyroxin and iodine.

Exophthalmos is seen in 65 percent of patients with primary diffuse toxic goitre. Reports are cited to indicate that the exophthalmos does not regress after the thyrotoxicosis is controlled. The pathogenesis of the exophthalmos is discussed and the importance of the following factors is evaluated.

Hypertrophy of orbital contents, particularly orbital fat is considered important. Relaxation of the rectus muscles, allowing the eye and orbital contents to protrude is probably not an important factor, since the role of the obliques is not satisfactorily explained. The importance of contraction of smooth muscle of the orbit is difficult to accept, since the orbital smooth muscle is vestigial in man. Edema of the orbital contents has been substantiated as a factor in exophthalmos. Orbital vasodilatation has not been proved to be a causative factor. Degenerative myositis, with increase in muscle size, can be at best only an inconstant cause of exophthalmos, since it is not uniformly present.

The action of the anterior pituitary

hormone probably plays a part. The work of Mulvany is discussed. The author concludes that although there appears to be a relationship between the exophthalmos and the anterior pituitary, its exact nature is as yet unknown.

Benjamin Milder.

14

EYELIDS AND LACRIMAL APPARATUS

Cristini, G. **Myoblastoma of the lid.** Rassegna Ital. d'Ottal., 1946, v. 15, May-June, pp. 207-223.

The dual nature of muscular tissue gives rise to the terms of leiomyoma and rhabdomyoma, depending upon whether the newgrowth is composed of smooth or striated muscle. The tumor described by Cristini was found in the lower lid of a woman 57 years of age and was classified as myoblastoma. It is the sixth one to be reported. The tumor develops slowly and insidiously and presents no characteristic clinical picture. Histologically the case is interesting because of the great variety of cell types and the complexity of structural features. Various phases of differentiation and maturation of the primative myoblastoma to the fibrocellular striated muscle are seen. (5 figures, bibliography.)

Eugene M. Blake.

Dobyns, B. M. **Studies on exophthalmos produced by thyrotropic hormone.** Surg., Gynec., and Obst., 1946, v. 82, March, pp. 290-300, May, pp. 609-617, June, pp. 717-722.

This study was undertaken to investigate the changes in the prominence of the eyes induced by the administration of various preparations of thyrotropic hormone and to correlate the exophthalmos with various tissue changes. In normal guinea pigs, thyroidectomy caused an increase in the prominence of the eyes. The intercorneal distance was used as a measurement of exophthalmos. At varying time intervals after the operation the following pituitary preparations were given and the exophthalmos measured. After antuitrin T definite exophthalmos occurred. After the purified thyrotropic product hyperplasia was noted but little or no exophthalmos. The crude extract produced an exophthalmos greater than the last drug but less than the first, and it also caused thyroid hyperplasia. The specific metabolic principle did not produce exophthalmos. Half the animals were castrated, which did not influence the development of exophthalmos. The antuitrin T produced gross and microscopic changes in the connective tissue in the orbit and elsewhere in the body. The fat deposits were depleted and partially replaced by a gelatinous material. Plasma fat and blood acetones were elevated and there was a polymorphonuclear leucocytosis. Skeletal and cardiac muscle fibres lost their striations and were found to contain multitudes of fat droplets. The theoretical and clinical significance of the micropathologic changes are discussed. (17 illustrations, 4 tables, references.)

Bennett W. Muir.

Grönvall, Herman. **A case of supernumerary caruncula lacrimalis.** Acta Ophth., 1944, v. 22, pt. 2, pp. 158-165.

A case of supernumerary caruncle in a seven-year-old child is reported. Because it apparently caused a sensation of chafing in the eyes, and consequent grimacing it was excised and found to have the histologic structure of a normal caruncle. A tabulated review of seven cases reported in the literature

is given and the pathogenesis discussed. (3 illustrations.) Ray K. Daily.

Lodge, W. O. **Observations on the eyelids.** J. Internat. Coll. Surgeons, 1946, v. 9, May-June, pp. 383-378.

The author mentions some forty affections of the lids. Spastic entropion may sometimes be cured by painting the lower lids with colodion. For paralytic ectropion he exposes the internal palpebral ligament and the frontal process of the zygomatic bone. A 0.003-inch tantalum wire is inserted horizontally through the lower lid and attached to the areas exposed. He uses a similar wire in the Motais and Hess types of operation for ptosis. (4 figures.)

I. E. Gaynon.

McArthur, G. A. D. **Some notes on West's operation (endonasal dacryocystostomy).** Med. Jour. Australia, 1946, v. 1, April 13, pp. 508-510.

The author describes his technique of endonasal dacryocystostomy. He removes a small portion of the medial wall of the sac through the frontal process of the maxilla. Failure occurs when the sac is too small, an inadequate opening is made, and if there is stenosis of the junction of the canaliculus and sac. Of 42 operations 35 were successful.

I. E. Gaynon.

Stenbeck, Anna. **A follow-up of dacryocystorhinostomies.** Acta Ophth., 1944, v. 22, pt. 1, pp. 27-35.

This is an analysis of the surgical experience at the Sabbatsberg Hospital during the five-year period from 1936 to 1941. One hundred and seventy external operations were performed, of which 134 could be followed. In 116 cases the lacrimal passages were patent on irrigation, and 18 were impermeable. Most of the patients with patent lacrimal passages had no symptoms. A few had epiphora only in the wind. Five had constant epiphora; in two of these the lower canaliculus was obstructed before the operation; one had a hyperplastic rhinitis, and in two the continuous epiphora in spite of patency of the lacrimal passages could not be explained. Of the 18 cases impermeable to irrigation 15 were normal when discharged, 3 developed obstruction shortly, 6 after two months, and 5 about one and one half years after the operation. In one patient the canal was patent for five years, when conjunctivitis, followed by an infection in the sac, resulted in an obstruction with dense tissue. In three patients the data on the recurrence of symptoms could not be established. Three patients were operated upon a second time, one externally and two intranasally; the connective tissue blocking the lacrimonasal opening was removed. A division of the material into four groups shows satisfactory results in 79.4% of stenosis, 87.8% of dacryocystitis, 73% of phlegmons, and 33.3% of pericystitis. It appears that the prognosis is best in dilated sacs, regardless of their content. Because the immediate post-operative results are better than the final, it is important to follow the patients for some time.

Ray K. Daily.

Svoboda, J. **Surgical treatment of lacerations of the lower lacrimal canals.** Lekarske Listy, 1946, v. 1, July 1, pp. 307-308.

Lacerations of the lower lacrimal canaliculus were corrected with the aid of the following operation in 53 patients. A probe-like wire is passed through the disrupted canal, after sutures have been placed in the conjunctiva but not tied. Then the edges of the laceration are stitched together

and the knots tied. It is important that the wire enters the nasolacrimal duct. The wire is retracted gradually during the postoperative period.

O. Felsenfeld.

Thygeson, Phillips. **The etiology and treatment of blepharitis: a study in military personnel.** Military Surg., 1946, v. 98, March, pp. 191-203.

Blepharitis was the most common external eye infection seen in military personnel. Laboratory and clinical studies of 350 cases of blepharitis indicate that the three important types are the staphylococcic, the seborrhoeic blepharitis, and the diplobacillary. Staphylococcic blepharitis is often unilateral, and is often associated with chalazion, hordeolum, and ulceration. It is characterized by small hard scales, which are tenacious and difficult to remove. An associated keratoconjunctivitis is almost the rule. Temporary or permanent loss of cilia, and associated otitis externa, impetigo, sycosis barbe and acne vulgaris are common. There is burning, itching, and photophobia.

With seborrhoeic blepharitis, there is seborrhea capitis, and usually an associated seborrhoeic dermatitis of brow and ears, the lesion is always bilateral, nonulcerative, and squamous, the scales are greasy and easy to rub off, and associated conjunctivitis is minimal if present. There are no complicating inflammations. The skin gives evidence of increased seborrhea, discomfort is minimal.

Diplobacillary blepharitis is characterized by maceration of the skin at the inner and outer canthus, and associated conjunctivitis. The infection is superficial, there is no ulceration, and no inflammation of the Meibomian glands.

The finding of budding yeast forms, pityrosporum ovale, was considered diagnostic of seborrhoeic blepharitis. Routine bromicroscopic examinations of the lid margin in chronic conjunctivitis revealed a high incidence of mild and subclinical blepharitis, usually staphylococcic. There is no evidence that vitamin deficiency, refractive error or allergy play significant roles.

I. E. Gaynon.

Torti, M. **Congenital lacrymal fistula.** Rassegna Ital. d'Ottal., 1946, v. 15, no. 1 and 2, p. 69.

Torti describes two cases of unilateral fistula of the lacrymal sac, one of which was definitely of congenital origin, the other probably inflammatory in nature. His conclusions are based upon histological studies of the excised tissue. Congenital fistula is caused by a supernumerary canaliculus and arises at the same period of development as the canaliculi. (4 figures.)

Eugene M. Blake.

15

TUMORS

Blake, E. M. **Cultivation of human tumor in the anterior chamber of the guinea-pig's eye.** Amer. Jour. Ophth., 1946, v. 29, Sept., pp. 1098-1106. (8 figures, references, discussion.)

Blegvad, Olaf. **Myxoma of the orbit.** Acta Ophth., 1944, v. 22, pt. 2, pp. 131-140. (See section 13, Eyeball and orbit.)

Byrn, Willy. **Three cases of hemangioma of the subconjunctiva.** Acta Ophth., 1944, v. 22, pt. 2, pp. 166-175. (See Section 5, Conjunctiva.)

Cristini, G. **Myoblastoma of the lid.** Rassegna Ital. d'Ottal., 1946, v. 15, May-June, pp. 207-223. (See Section 14, Eyelids and lacrimal apparatus.)

Godtfredsen, Erik. **Choroid metastases in chorionepithelioma of the testicle.** Acta Ophth., 1944, v. 22, pt. 3, pp. 300-310. (See Section 7, Uveal tract, Sympathetic disease and aqueous humor).

Godtfredsen, Erik. **The frequency of secondary carcinomas in the choroid.** Acta Ophth., 1944, v. 22, pt. 4, pp. 394-400. (See section 7, Uveal tract, sympathetic disease, and aqueous humor.)

Godtfredsen, Erik. **Ophthalmologic and neurologic symptoms of malignant naso-pharyngeal tumors.** Acta Ophth., 1944, supplement 22, pp. 373.

This exhaustive monograph is based on a review of the literature and on a study of 454 case histories from the largest radiologic clinics of Denmark and Sweden, during the period from 1927 to 1942. The clinical symptoms are described in great detail. Of interest to the ophthalmologist are the patients with ophthalmoneurologic symptoms, which constitute 38 percent of this material. Usually these symptoms appear early if they appear at all. The nerves most frequently involved were the fifth cranial nerve and the eye nerves, separately or jointly. Half of the ophthalmo-neurologic patients presented purely ophthalmologic symptoms, such as muscle paralysis, optic tract lesion, exophthalmos, and Horner's syndrome. These findings indicate that a malignant naso-pharyngeal tumor should be suspected in the presence of these symptoms, even if local nasopharyngeal symptoms are absent. In these patients there was an average period of 11 months between the onset of symptoms and a correct diagnosis. An exhaustive examination of the nasopharynx should lead to an earlier diagnosis, earlier institution of proper treatment, and a better prognosis. An analysis of microscopic preparations in 458 cases reveals a difference between those with and without ophthalmoneurologic symptoms. The former contain a relatively greater number of squamous-cell carcinomas and cylindromas, and a smaller number of plasmocytomas and lymphosarcomas than the latter.

The therapeutic results show that sarcomas and lympho-epitheliomas are fairly radio-sensitive, and that with modern radiation therapy 22 percent of patients were free from symptom for five years, and three fourths of all become free from symptom after treatment. (53 illustrations, 30 tables.)

Ray K. Daily.

Penido Burnier and Salles Monteiro. **Teratoma of the orbit.** Arquivos do Instituto Penido Burnier, 1945, v. 7, Dec., pp. 114-128.

The authors found the subject dealt with merely in articles of the French and American encyclopedias of ophthalmology and in a few scattered articles in ophthalmologic reviews. They report the case of a two-months-old female child born at term, of normal birth. Three previous pregnancies had been normal and had been completed at term. There had been one spontaneous abortion at a few months, preceding the last completed pregnancy. The mother reported that the child had been born with the orbital tumor practically of the same size as it manifested at the age of two months. X-ray examination showed a great increase in size of the left orbit. Puncture at two different levels was negative. The puncture needle traversed trabecular areas sometimes of clayey consistency. After making the differential diagnosis from

hernias of cranial content, the tumor was successfully excised. It measured 6.2 by 6.0 by 4.5 cm., and weighed 92 gm. (10 illustrations, including 4 photomicrographs, references.)

W. H. Crisp.

Quintana, Juan. **Orbital Mixoma.** Arch. de la Soc. Oft. Hisp.-Amer., 1945, v. 5, May, pp. 346-351. (See Section 13, Eyeball and orbit.)

Zeeman, W. P. C. **The diagnosis of a flat sarcoma of the choroid and the histological substratum of the changes observed with the ophthalmoscope.** Acta Ophth., 1943, v. 21, pts. 1-2, pp. 47-60. (See Section 7, Uveal tract, Sympathetic disease and aqueous humor.)

16

INJURIES

Alvis, Bennett Y. **The use of the Berman locator in removal of intraocular foreign bodies.** South. Med. Jour., 1946, v. 39, Feb., p. 125.

This instrument has helped to differentiate a magnetic from a non-magnetic foreign body, to locate a magnetic foreign body, and to follow its changing position during the course of its removal.

Seven cases are briefly described and discussed. Important surgical details are mentioned and the exact localization of the foreign body is reported, at times with an accuracy so great as to obviate the need to introduce the magnet's tip into the vitreous.

The size of the foreign body and its distance from the locator has a definite influence on the latter's response. Posteriorly located small foreign bodies bring a response if the globe is rotated so as to shorten the distance between the locator and the foreign body.

F. M. Crage.

Bertotto, E. V. **Symblepharon with serious effect on motility.** Anales Argentinos de Oft., 1945, v. 6, July-Aug.-Sept., pp. 98-100.

After an injury to the left eye by a machine-screw, conjunctival synechiae formed which prevented movement of the eye inward and upward. As a result, diplopia manifested itself in these directions of gaze. After two operations to relieve the symblepharon the diplopia disappeared and normal ocular motility returned. Edward Saskin.

Broendstrup, Poul. **Two cases of temporary siderosis bulbi with spontaneous resorption and without impairment of function.** Acta Ophth., 1944, v. 22, pt. 3, pp. 311-316.

In the first patient a small intraocular foreign body was discovered two years after the injury. The patient complained of failing vision and discoloration of the iris. There was incipient cataract and siderosis of the iris. The foreign body was not removed. The siderosis progressed for a few months, and then gradually receded until six years later when the color of the iris had become normal. Eleven years after the first examination the foreign body could not be demonstrated roentgenoscopically. The second patient, a man, 19 years of age, presented unmistakable clinical signs of an ocular perforation and pronounced siderosis of the iris without a history of trauma and without a demonstrable foreign body. In the course of 18 months he developed a mature cataract which was successfully needled. Fourteen years later all evidence of siderosis had disappeared.

It is pointed out that the result might be better if small intraocular foreign bodies were left to spontaneous absorption. Ray K. Daily.

Brueckner, R. **A case of thrombosis of the central retinal vein after a trauma.** Ophthalmologica, 1945, v. 109, Apr.-May, pp. 203-211. (See Section 10, Retina and vitreous.)

Casanovas, J. **Radiographic methods for the localization of foreign bodies of the visual apparatus.** Arch. de la Soc. Oft. Hisp.-Amer., 1945, v. 5, May, pp. 327-337. (See Section 1, General methods of diagnosis.)

Chamberlain, W. P. and Boles, D. J. **Edema of cornea precipitated by quinacrine (atabrine).** Arch of Ophth., 1946, v. 35, Feb. pp. 120-134. (See Section 6, Cornea and sclera.)

Chulia, Vincente. **A curious case of intraocular foreign body.** Arch. de la Soc. Oft. Hisp.-Amer., 1945, v. 5, May, pp. 368-370.

A large piece of steel had penetrated the cornea and lodged on the iris without damaging the lens. The foreign body was removed by means of iris forceps through a limbal incision.

J. Wesley McKinney.

Ciello, Alcides del. **Ocular affections produced by poisonous animals and plants.** Arquivos Brasileiros de Oft., 1946, v. 9, Feb., pp. 10-21.

A brief recital of such disturbances, with a page of references.

W. H. Crisp.

Cruise, Richard. **Preventable blindness in war.** Trans. Ophth. Soc. U. Kingdom, 1944, v. 64, p. 165.

Modern warfare with explosives causes puncture wounds of the eyes, panophthalmitis, foreign bodies in the globe, lacerations of the cornea or sclera, prolapse of the iris, and concussion injuries to lens or retina. To prevent them the author presented a visor that consists of a perforated sheet of 22-gauge duralumin. It can be attached to the helmet and can be pulled down easily. Vision is not reduced by the visor. It weighs 0.395 lb. (13 illustrations.) Beulah Cushman.

Filippi Gabardi, E. **An electric needle for extraction of foreign bodies in the cornea.** Rassegna Ital. d'Ottal., 1946, v. 15, May-June, pp. 224-226.

The author describes an ingenious foreign body needle which does away with the need of an assistant. A slender tube containing a condensing lens and a light at the end is attached to a pocket flashlight battery by a flexible cord. At the light end of the tube a collar is affixed into which either a needle or gauge can be inserted. With this instrument the operator has a bright, condensed light and a foreign-body spud, and one hand free to separate the eyelids. (2 figures.) Eugene M. Blake.

King, E. F., and Samuel, E. **Fractures of the orbit.** Trans. Ophth. Soc. U. Kingdom, 1944, v. 64, pp. 134-154. (See Section 13, Eyeball and orbit.)

Luz, B. da, and Sebas, S. R. **Foreign body tolerated for eleven years.** Rev. Brasileira de Oft., 1946, 4th yr. June, no. 4, pp. 313-316.

The patient was a mechanic aged 40 years, the sight of whose right eye had been lost in consequence of penetration of the eye by a fragment of metal 11 years previously. He had

many periodic attacks of ocular and periorbital pain, varying in intensity. There was no light perception. In the enucleated eye the metallic foreign body was found embedded in the sclera 3 mm. behind the equator of the eye. The lens was absent, probably having been removed in an earlier operation to which the patient made vague reference. (References.) W. H. Crisp.

Marner, Else. **A case of ocular chalcosis with spontaneous resorbtion of the copper and disappearance of chalcosis.** Acta Ophth., 1945, v. 23, pt. 2, pp. 171-174.

This is a follow-up report of a case reported by Kjerrumgaard in 1941. A 10-year-old boy had both eyes injured in 1937 by the explosion of a percussion cap. X-ray examination revealed two small metallic foreign bodies in each eye. Three years after the injury there was bilateral chalcosis. Eight years after the injury no foreign bodies could be demonstrated in the left eye by X ray, and the chalcosis in that eye had practically disappeared; there were only faint traces of the previously found disk-shaped central opacity on the anterior surface of the lens. The chalcosis on the right side persisted, but one foreign body was no longer visible. Ray K. Daily.

Pinkerton, O. D. **Traumatic liporrhagia retinalis.** Arch. of Ophth., 1946, v. 35, Feb., pp. 176-178.

The history of a case of traumatic liporrhagia retinalis or Purtscher's disease in an 11-year-old Filipino boy is presented. The boy was struck by a vehicle. The injury consisted of a severe lacerated wound of the left temporal and frontal areas and the left external canthus, compound, comminuted, complete fracture of the left zygoma, and contusions of both sides of the face, the chest, and the upper portion of the abdomen. Within six hours the vision of the right eye was limited to perception of light peripherally. A massive yellow extravasation with hemorrhages was observed in the fundus. Within a month there was complete absorption of the exudate and hemorrhage except for a small amount between the nerve head and macula. A marked pallor of the nerve developed. Vision was limited to counting fingers at three to four feet in the temporal and superior fields only. Abscess of the lung developed at a late date.

John C. Long.

Swanson, C. A. and Stewart, R. A. **Causes of uniocular and binocular blindness in the U. S. Navy and U. S. Marine Corps in World War II.** Sight-Saving Review, 1946, v. 16, Spring, pp. 36-46.

The treatment of ocular injuries during World War II were characterized by improved care mainly because of chemotherapy. Of 119 cases of bilateral blindness, 84 resulted from trauma, and 35 from medical causes. Methyl alcohol poisoning was the cause in 19 of the latter. Of 640 cases of unilateral blindness, 464 resulted from trauma. Two-thirds of the intraocular foreign bodies were magnetic. The Berman locator is useful in determining this fact. Foreign bodies up to 2 mm. in diameter usually leave a useful eye. Sympathetic ophthalmia occurred five times after removal of intraocular foreign bodies. I. E. Gaynon.

Uhde, G. I. **Arsenical eye burns.** Amer. Jour. Ophth., 1946, v. 29, Sept., pp. 1090-1093. (5 figures.)

Uhde, G. I. **Mustard-gas burns of**

human eyes in World War 11. Amer. Jour, Ophth., 1946, v. 29, August, pp. 929-938. (6 figures, 7 tables.)

17

SYSTEMIC DISEASES AND PARASITES

Arroyo, Manuel. **Onchocercosis and its ocular complications.** Rev. Brasileira de Oft., 1946, 4th yr., June, No. 4, pp. 285-295.

The author summarizes the first classical report of a case as given by Rodolfo Robles, including the following symptoms: reddening of the conjunctiva; iritis; the formerly brilliant and transparent cornea becoming dull and without gloss; tiny leukomas (as though the patient had suffered from an ulcerative keratitis); constant headache and periorbital pain, and marked diminution of visual acuity. In honor of the distinguished ophthalmologist referred to, who died recently, the present author urges that the disease should be known as Robles's disease.

W. H. Crisp.

Arumi, J. **Subconjunctival cysticercus.** Arch. de la Soc. Oft. Hisp.-Amer., 1945, v. 5, May, pp. 339-345.

A case of a cyst that was excised and studied histologically is reported.

J. Wesley McKinney.

Brueckner, R. **A case of Sjögren's syndrome, successfully treated with Perandren.** Ophthalmologica, 1945, v. 110, July-Aug., pp. 37-42. (See Section 6, Cornea and sclera.)

Cassady, J. V. **Uveal blastomycosis.** Arch. of Ophth. 1946, v. 35, Feb., pp. 84-97.

A 64-year-old white man was first seen because of polyarthritis and cutaneous lesions. During the course of severe and multiple systemic manifestations, a uveitis developed in the right eye. Posterior synechiae were present and a yellowish, tubercle-like nodule was seen at the pupillary margin of the iris and another at the base. Biopsy and culture of material from the cutaneous lesions yielded a fungus identified as Candida parapsilosis. Attempts to culture this organism from the aqueous were unsuccessful. The patient's condition grew worse and he died approximately one year after the onset of the joint symptoms. Autopsy showed extensive blastomycotic lesions in the skin, lungs, prostate, kidneys, bones, and eyes. Histologic study of the eye showed tubercles in the deep corneal abscesses, areas of necrosis, lymphocytes, plasma cells, epithelioid cells, and giant cells. Giant cells which had engulfed the double-contoured bodies of fungus, some of which were budding, were found throughout the mass in great numbers..

Should eye changes become apparent during the course of endogenous blastomycosis (Gilchrist's disease) the author suggests the withdrawal of the plasmoid intraocular fluid for cytologic examination and culture. (11 illustration.) John C. Long.

Contino, F. **Surgical treatment of subretinal cysticercus.** Rassegna Ital. d'Ottal., 1946, v. 15, May-June, pp. 165-181.

Since all attempts to destroy an intraocular cysticercus by medical means appear to be useless the treatment must be surgical. After reviewing all the methods employed to destroy the parasite within the eye, the author describes two eyes in which he succeeded in killing the cysticercus by means of diathermy coagulation with the Weve

technic. The treatment permitted the retention of the globe but vision was almost nil. (2 figures, bibliography.)

Eugene M. Blake.

Davenport, R. C. **Ocular psychoneuroses.** Trans. Ophth. Soc. United Kingdom, 1944, v. 64, p. 24.

The incidence of ocular psychoneurosis is difficult to estimate but patients may be roughly grouped in three divisions: those with an obvious organic defect that causes the symptoms; those with an inadequate organic basis for their troubles; and an intermediate group in which the patients have an organic lesion upon which an element of neurosis is overlaid.

The large majority of patients present enough of their personality for the ophthalmologist to make adequate judgment before he proceeds to treatment. Much of the judgment may be made as the history of the complaint is given.

The large majority of patients have hysteria or one of the anxiety states and squints afford a wide field for the assessment of the psychopathic factor.

A number of functionally blind were received after the retreat from Flanders and most of them recovered their vision after rest and reassurance, but night terrors persisted. Of four others sent to St. Dunstan's Hospital, three had one seeing eye and the fourth a large error of refraction. Conscious malingering was rarely found.

The author urges the importance of assessing the psychological factor in all eye patients. Beulah Cushman.

Doggart, J. H. **Ocular psychoneurosis.** Trans. Ophth. Soc. United Kingdom, 1944, v. 64, p. 29.

The psychoneurotic patient with his lowered threshold for anxiety often collapses with panic at the mere thought of failing sight; and fear, once it has gripped him, may be aggravated by the many menacing advertisements.

The commonest complaints in ocular psychoneurosis are failing vision, spots or flashes of light, intolerance of glares, double vision and difficulty in focusing, transient blurring, and aching of the eyes.

The author found that elaborate traps for the malingerers seldom justified the time expended, as most malingerers are stupid enough to give themselves away. The borderline between conscious pretense and psychoneurotic inhibition cannot always be established, and in any event no disciplinary action can be taken on a charge of foxing over test-types.

He concluded with Tostevin that ocular defects were seldom the primary cause of failure in air cadets. The author also believes that the correlation of the different branches of medicine which is generally desirable is particularly needed between neuropsychiatry and ophthalmology. The final disposal of serious problems should be left to the neuropsychiatrist.

Beulah Cushman.

Gillespie, R. D. **Ocular psychoneurosis.** Trans. Ophth. Soc. United Kingdom, 1944, v. 64, p. 41.

All the fundamental lessons of psychosomatic medicine can be applied to or deduced from functional disorders of the visual apparatus as its functions include sensation, voluntary movement, and involuntary movement of unstriped muscle.

The dependence of many ophthalmological tests upon willing co-operation of the patient gives scope for malingering but the infinite capacity of the human race for self-deception

makes the additional gift of malingering almost unnecessary.

The most used function may often be made abnormal by hysteria or anxiety neurosis. The only common hysterical disorders of eye movement, is failure to converge, based on a lack of desire to look. Failure to accommodate can also be hysterical.

Sixty-six air crews undergoing orthoptic treatment were subjected to psychiatric examinations and 40 were found to have in some degree the same characteristics that were found in air crews that broke down with frank psychoneurotic disorders.

Anxiety symptoms may arise in someone of average psychological constitution where external stress is great or motivation to fly is inadequate.

The author is not willing to go as far as some who say that the mentality of everyone who has heterophoria is abnormal. Beulah Cushman.

Grossman, E. E. **Conjunctivitis associated with erythema multiforme bullosa.** Amer. Jour. Ophth., 1946, v. 29, Sept., pp. 1146-1149. (References.)

Haar, M. **Reiter's disease.** Acta. Ophth. 1945, v. 23, pt. 2, pp. 143-150. (See Section 5, Conjunctiva.)

Haar, M. **Ophthalmomyiasis interna posterior.** Acta Ophth., 1945, v. 23, pt. 2, pp. 135-141.

The literature on 30 published cases is reviewed and a new case reported. While spending a vacation in the mountains a twelve-year-old boy developed an iridocyclitis of the right eye, and during the course of the disease a sharply circumscribed grayish white shiny body could be seen in the vitreous below and nasal to the papilla. It was interpreted as a larva of hypoderma lineatum. The lens became dislocated. Within a year the media cleared, vision became normal, and the appearance of the larva indicated that it was being absorbed. Within that period the child had edematous swelling on the head and face, nodules on the scalp, and eosinophilia (15 percent). Spontaneous recovery, without removal of the larva is reported in one other case in the literature. Ray K. Daily.

Johnson, H. C. **Retinal venous sheathing in multiple sclerosis; report of a case.** Amer. Jour. Ophth., 1946, v. 29, Sept., pp. 1150-1151. (3 figures, references.)

Kravitz, Daniel. **Infections and reflex disorders of the eye from dental affections.** Amer. Jour. Ophth., 1946, v. 29, Sept., pp. 1135-1145. (References.)

Lech Junior. **Vanadium in ocular syphilis.** Arquivos do Instituto Penido Burnier, 1945, v. 7, Dec., pp. 204-211. (See Section 2, Therapeutics and operations.)

Milder, Benjamin, **The eye examination in the differential diagnosis of the disoriented patient.** Amer. Jour. Ophth., 1946, v. 29, August, pp. 953-967. (2 tables, references.)

Morgan, O. G. **Ocular psychoneurosis.** Trans. Ophth. Soc. United Kingdom, 1944, v. 64, p. 52.

The author describes several patients with self-inflicted artefact conjunctivitis who responded to psychotherapy. Beulah Cushman.

Prezidio de Figueiredo, Nicanor. **A case of ocular avitaminosis.** Rev. Brasileira de Oft., 1946, v. 4, June, pp. 317-324.

A man of 26 years, in an artillery encampment, showed chronic irritation to which the author gives the title "blepharokeratoconjunctivitis." Failure of previous modes of treatment, and marked improvement under a Brazilian vitamin preparation, convince the author that the ocular disturbance was due to deficiency in riboflavin.

W. H. Crisp.

Richards, J. M. and Romaine, H. H. **Keratoconjunctivitis sicca.** Amer. Jour. Ophth., 1946, v. 29, Sept., pp. 1121-1125. (7 figures, references.)

Rundle, F. F. and Wilson, C. W. **Development and course of exophthalmos and ophthalmoplegia in Graves' disease with special reference to the effect of thyroidectomy.** Clinical Science, 1945, v. 5, Dec., pp. 177-194. (See Section 13, Eyeball and orbit.)

Saenz Canales, José. **The vitreous body in some ocular localizations of the cysticercus.** An. de la Soc. Mexicana de Oft. etc., 1945, v. 20, April-June, p. 55.

Much of the article is taken up with a discussion of vitreous structure, and of the literature of the subject since Graefe, who in his Archiv gave an excellent description of the ophthalmoscopic appearance. The author of the present article gives a review of the ophthalmoscopic appearance in subretinal localization of the cysticercus, including the innumerable glistening crystals whose appearance varies with every movement of the vesicle. A little later come the spots commonly associated with the names Liebreich and Cirincione. These are roundish spots of variable size, comparable to little drops of dirty oil, or to the precipitates of descemetitis. Pseudomembranes frequently follow. The various stages of disintegration of the vitreous are attributed by the author to inflammation, degeneration, and allergy. (Four photomicrographs, references.)

W. H. Crisp.

Sardana, M. N. **Ocular manifestations of avitaminosis in adults.** Indian Med. Gazette, 1946, v. 81, p. 188-193.

Five hundred cases of avitaminosis with ocular symptoms were observed in 1943 at the Indian Prisoners of War Hospital in Singapore under Japanese occupation. Under the circumstances the methods of diagnosis and treatment were meager. Treatment consisted of the feeding of rice polishings, rice water, red palm oil, and marmite.

Vitamin A deficiency was found in 159 patients. The chief complaints were night blindness and itching and dryness of the eyes. The cornea was insensitive in 81 percent of the patients, there were corneal ulcers in 2 percent, disciform keratitis in 2 percent, and blepharitis in 5 percent. The pupils were dilated and visual acuity was impaired.

Deficiency of vitamine B_1 was found in 220 patients. They complained of decreased vision, photophobia, and of a burning sensation. The pupils were normal in size, reacted well to light, and were sluggish in accommodation. The fields were slightly contracted and two percent of the patients had optic nerve atrophy.

The 121 patients who had deficiency of riboflavine complained of hazy vision in the sun. The pupils were slightly dilated and reacted sluggishly to light. The visual acuity was reduced, accommodation was normal, and the fields were contracted in the upper and temporal regions. I. E. Gaynon.

Skydsgaard, Henning. **Polyarthritis urethritica simplex with eye symptoms. (Reiter-Freunds syndrome).** Acta Ophth., 1943, v. 21, pts. 1-2, pp. 107-118.

Four cases are briefly reported. The characteristic feature of this syndrome is the non-gonorrheal triad of urethritis, conjunctivitis, and arthritis. The conjunctivitis is the least conspicuous of the symptoms. This syndrome should be kept in mind when dealing with purulent conjunctivitis of unknown etiology, and in the differential diagnosis of exogenous gonorrheal conjunctivitis. Ray K. Daily.

Souza Queiroz, Leoncio de. **Ocular cysticercosis.** Arquivos do Instituto Penido Burnier, 1945, v. 7, Dec., pp. 129-150.

From 1913 to 1945, a total of 92 cases of ocular cysticercosis have been recorded in the Penido Burnier Clinic. The statistics relating to these cases are analyzed. They include subconjunctival, cysticercus of the anterior segment, of the vitreous, and subretinal. Other phases of the subject dealt with are the reaction of the complement fixation for cysticercosis, prognosis and prophylaxis, and treatment. A typical case of subretinal cysticercus in a woman of 28 years is detailed. The cyst was in the nasal sector, was located by diathermy puncture, and was extracted with very slight traumatism. Vision returned from 0.3 to normal. (12 illustrations, elaborate analytical statistical table, biblography.)

W. H. Crisp.

Stewart, D. S. **Ocular psychoneurosis.** Trans. Ophth. Soc. United Kingdom, 1944, v. 64, p. 54.

The author reviewed the histories of 131 patients who complained of headaches in a group of 231 psychoneurotic patients. He feels that every patient consulting an oculist is in a state of "eye consciousness." To succeed in unmasking a malingerer by optical trickery is creditable in so far as it helps to exclude an organic cause for the pretended amblyopia or spastic strabismus, but to dismiss the patient harshly without further consideration is as unsuitable as to kick away the crutches from a cripple.

Beulah Cushman.

Traquair, H. M. **Ocular psychoneurosis.** Trans. Ophth. Soc. United Kingdom, 1944, v. 64, p. 37.

The symptoms of the psychoneurotic eye patient are characterized by inconsistency in themselves and are not justified by the physical findings.

The diagnosis and treatment go together. As the diagnostic measures are carried out they impress the patient and pave the way for successful treatment. The study of the binocular visual field and of the field of vision of each eye separately are among the most useful tests. They should be repeated at 2 M.

The author feels that the chief cause of the psychogenic visual symptoms is fear and personal maladjustment. The chief elements in treatment are explanation, distraction, encouragement and "therapeutic conversation."

Beulah Cushman.

Weskamp, C. **Ocular syphilis.** Anales Argentinos de Oft., 1945, v. 6, Apr.-May-June, pp. 47-52.

The first part deals with generalities. This section is devoted to a discussion of extraocular syphilitic lesions and their therapy with arsenic, bismuth, and malaria.

The second part deals with specific

ocular syphilis. Primary optic atrophy is a result of neurosyphilis, and appears from 10 to 20 years after the initial lesion. It is frequently accompanied by the Argyll-Robertson pupil. Interstitial keratitis is the other sign that is virtually indicative of syphilis. Treatment of ocular syphilis depends upon the location of the lesion and the duration of the disease. Lesions that involve mesodermal structures in the iris, the choroid, and the sclera, respond to bismuth, arsenic, mercury. Lesions in the neural ectoderm such as optic atrophy, require fever therapy. The author describes penicillin as a new potential antiluetic measure.

Edward Saskin.

Winnicott, D. W. **Ocular psychoneurosis.** Trans. Ophth. Soc. United Kingdom, 1944, v. 64, p. 46.

The author gives an account of the ocular psychoneuroses of childhood. He asks for belief in the matter of the reality of feelings in a child and as an example quotes the experience of a friend whose childhood was spoilt by the remark of an eye surgeon. He told the child's mother in her presence that she has retinitis pigmentosa and would probably become blind. The child spent her childhood expecting blindness and did not begin to realize until she was 50 years of age that the surgeon was wrong. Children feel that they are the custodians of any part of their bodies and if they fail to keep their eyes healthy they feel they have failed in a trust.

Three groups of psychological symptoms are recognized: those shown by children whose personality structure is satisfactory; those that are associated with depression; and those associated with a defect of the structure of the personality.

Glasses quickly acquire a meaning to the child who wears them as they become part of the personality of the child.

Hysterical blindness is associated with guilt about seeing.

Depression in childhood is recognized as a mood and appears clinically in its form of common anxious restlessness or of a denial of depression by forced activity and liveliness. Along with this there are self destructive actions, deliberate or accidental, and also hypochondriacal worry over the body or its parts. Depression is very common among children and hypochondriacal worry joins with normal concern.

Hypochondria of the mother must be distinguished from that of the child. True reassurance comes from statement of facts.

Squint can have a purely psychological cause and the author describes three types: an external squint in which the two eyes do not work with one aim, and that is associated with a division in the personality; convergence that can be likened to thumb sucking; and a type that accompanies a phase of acute introversion.

Beulah Cushman.

Woods, A. C. **The ocular changes of primary diffuse toxic goiter.** Medicine, 1946, v. 25, May, pp. 113-154. (See Section, 13, Eyeball and orbit.)

18

HYGIENE, SOCIOLOGY, EDUCATION, AND HISTORY

Cordes, F. C. **Ophthalmology's post war responsibilities and opportunities.** Jour. Amer. Med. Assoc., 1946, v. 131, Aug. 24, pp. 1395-1397.

A three or four year residency at a medical center is ideal. A basic course

of six or eight months followed by a year or more of carefully supervised clinical work will help to make a safe ophthalmologist. Training may also be acquired through preceptorship and association in private practice with a qualified ophthalmologist. The basic course plus supervised reading, as outlined in the home study course, is essential. A number of three-year residencies and refresher courses should be arranged for training of men from Central and South America.

I. E. Gaynon.

Harrowes, W. M. **Psychological reactions in war blinded.** Brit. Med. Jour., 1946, no. 4464, July 26, pp. 129-130.

Forty patients were studied. All had a retrospective flattening out of a reactive depression. Thirty-five percent developed a classical tension depression characterized by fault finding, uncooperativeness, undue slowness of learning, and rejection of all suggestions. One patient over-compensated and the others gradually became stabilized.

I. E. Gaynon.

Hinshaw, J. H. **Legal ophthalmology.** Amer. Jour. Ophth., 1946, v. 29, Sept., pp. 1112-1118. (Discussion.)

Lech Junior. **Twenty-five years of activity of the Penido Burnier Institute.** Arquivos do Instituto Penido Burnier, 1945, v. 7, Dec., pp. 5-29.

With ample statistics, and 12 architectural and personal photographs, this 25-page article reviews the history of the institution. W. H. Crisp.

Pinson, E., and Chapanis, A. **Visual factors in the design of military aircraft.** J. Aviation Med., 1946, v. 17, April, pp. 115-122.

In a study by the Air Technical Service Command, the importance of diurnal visual acuity, depth perception, visual fields, and night vision are recognized. Aircraft should be designed so as to allow these human factors to be at their maximum efficiency. The importance of mechanical design, and of improved optical materials and their use, is stressed. (5 figures, 2 tables, references.) Bennett W. Muir.

Rochon-Duvignon A. and Aubaret. **Jacques Daviel: His life and the discovery of cataract extraction.** Ann. d'Ocul., 1946, v. 179, Jan., pp. 1-23.

Monday, April 8, 1745, was an epoch-making day in ophthalmology. A small man of about fifty had successfully performed the first complete cataract extraction in history. This issue of the Annales commemorates the two hundredth anniversary of this great event and is largely dedicated to the memory of the father of French ophthalmology.

Daviel conceived the need of a complete cataract extraction about 1741, when he unsuccessfully performed a bilateral reclination for cataract on the eyes of the hermit of Aguiles. In the second eye fragments of the lens cortex fell into the anterior chamber and this occurrence prevented his pushing the lens backward and downward into the vitreous. He apparently knew that Petit had previously removed dislocated lens matter from the anterior chamber through an incision at the lower limbus.

His first three operations, reported in 1743, were performed with a bistoury-like knife, a needle, and a probe-like instrument on a handle. Four years of effort and experiment resulted in his improved technique. An incision was made in the lower part of the limbus

with a straight keratome-like knife and enlarged with a curved scissors. The capsule was then opened with a cutting needle, the precursor of the modern cystotome. Through a round pupil the lens was expressed into the anterior chamber from which it was removed with a spoon which still bears his name.

In the following 11 years Daviel reported having performed 354 cataract extractions of which 305 were successful. Among his royal patients were the Royal Princess Palatinate and King Ferdinand VII of Spain. Louis XV of France, interested, ordered him to operate on the eyes of a dog, after which he made him oculist to the King.

Daviel was born in Normandy between 1693 and 1696. After completing his medical studies at Hotel Dieu in Paris, he began practicing in Marseilles. When an epidemic of plague had become catastrophic in the Toulon area Daviel volunteered for medical service there, and was cited for his work, courage, and devotion to duty. Upon returning to Marseilles, an attempt to rescind his hospital appointment was made by the city officials for medico-political reasons. At about that time he took up ophthalmology. In 1744 he moved to Paris where he practiced until shortly before his death. In 1762 Daviel developed laryngeal paralysis. He went to Geneva because of his health and there he died September 30, 1762, where his body still remains.

Charles A. Bahn.

Smith, V. M. **Rehabilitation of the partially seeing.** Sight-Saving Review, 1946, v. 16, Spring, pp. 31-35.

Evaluation of eyesight should be based on the central visual acuity of each eye, binocular vision, muscle action, peripheral vision, and color vision. Illumination should be adequate, and free from glare. Work should be arranged to prevent ocular fatigue and should be selected with consideration of the patient's disability. Braille should not be taught until it is necessary. The ophthalmologist should recommend in his report what the patient may do. I. E. Gaynon.

19

ANATOMY, EMBRYOLOGY, AND COMPARATIVE OPHTHALMOLOGY

Katzin, H. M. **Photography of the external eye.** Arch. of Ophth., 1946, v. 35, May, pp. 514-518.

Photographic reproduction of the eye has become an indispensable part of teaching, research, and medical records. The mechanical problems involved are different from those found in general photography or photomicrography because the eye is neither gross nor microscopic in size. The problems are really those of low power photomicrography. Further, because of the problem of blinking, particularly in photophobic eyes, the light source should be synchronized with the shutter of the camera, and the time of exposure must be minimal. Many types of cameras have been used for this purpose.

A discussion of the film, lenses, depth of focus, focusing, and lighting is given and the camera setup used by the author is described.

R. W. Danielson.

Stone, L. S. **Return of vision in transplanted adult salamander eyes after seven days of refrigeration.** Arch. of Ophth., 1946, v. 35, Feb., pp. 135-144.

The adult eye of the salamander may be transplanted with a return of vision. A new lens is regenerated from the

dorsal pupillary margin of the iris and a new retina from the undegenerated ciliary margin of the old retina. Seventy enucleated eyes of the adult salamander, Triturus viridescens, were refrigerated at a temperature of from 0 to 8°C. in sterile Ringer solution for periods ranging from two to fourteen days and were then transplanted into freshly denuded orbits of new hosts. After two days of refrigeration at 8°C. some of the eyes eventually became normally functioning organs. Refrigeration for longer than two days required a lower temperature (4 to 6°C.) to insure survival of the graft and successful transplantation. Eyes isolated as long as seven days at this temperature were successfully grafted, and return of vision was demonstrated a little over three months after they were transplanted. These eyes remained functional and were normal in appearance one year after they were grafted. John C. Long.

Warkany, J. and Schraffenberger, E. **Congenital malformations induced in rats by maternal vitamin A deficiency.** Arch. of Ophth., 1946, v. 35, Feb., pp. 150-169.

When female rats were raised and bred on a dietary regimen which leads to extreme vitamin A deficiency during pregnancy, congenitally deformed offspring were obtained. There were various defects of the skeleton and some defects of the soft tissues. Sections of the eyes showed a fibrous retrolenticular membrane in place of the vitreous in every specimen. In addition there were frequently colobomas, eversion and abnormal structure of the retina, rudimentary development of the iris and of the ocular chambers, defects of the cornea and of the conjunctiva and lack of fusion of the lids. These congenital abnormalities consisted partly of structures arrested in early ontogenetic stages and partly of formations that do not correspond to normal embryonic conditions. When the maternal diet was supplemented with vitamin A during pregnancy, the eyes of the young were normal. John C. Long.

NEWS ITEMS

Edited by DONALD J. LYLE, M.D.
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News items should reach the editor by the twelfth of the month

DEATHS

Dr. Carl Bishop, Plainville, New Jersey, died July 27, 1946, aged 46 years.

Dr. Joseph Marie Louis Bruno, Brooklyn, New York, died July 14, 1946, aged 52 years.

Dr. Phillips Eagleton, Newark, New Jersey, died September 11, 1946, aged 80 years.

Dr. Charles Willard Geiger, Kankakee, Illinois, died July 19, 1946, aged 75 years.

Dr. Gaylord Crawford Hall, Louisville, Kentucky, died June 16, 1946, aged 66 years.

Dr. Thomas D'Arcy McGregor, Buffalo, New York, died July 14, 1946, aged 52 years.

Dr. Joseph Louis Nocentini, Philadelphia, Pennsylvania, missing in action January 12, 1944, determined dead June 13, 1945, aged 34 years.

Dr. Robert Von der Heydt, Chicago, Illinois, died September 18, 1946, aged 71 years.

MISCELLANEOUS

The first international fellowship to be granted by The Eye-Bank for Sight Restoration, Inc., 210 East 64th Street, New York 21, has been announced by Mrs. Henry Breckinridge, executive director.

The candidate, chosen because of his outstanding qualifications, to be awarded this fellowship is an ophthalmologist of the Hebrew University in Palestine. He will receive postgraduate training in ophthalmology and research work in problems relating to the cornea at the Wilmer Institute, Johns Hopkins University, Baltimore, Maryland.

Dr. Grant Balding, 117 East Colorado Street, Pasadena, California; Dr. Paul L. Cusick, 1108 Stroh Building, Detroit, Michigan; Dr. Frederick C. Cordes, 384 Post Street, Dr. Max Fine, 350 Post Street, San Francisco, California, and Dr. L. Connor Moss, 1710 Rhode Island Avenue, N.W., Washington, D.C., have been named consultants in ophthalmology to the Secretary of War.

Major Gen. Norman T. Kirk, the Surgeon General of the Army, under whose direction the Armed Services medical consultant program was initiated during the war, said that the appointment of civilian consultants will augment the Army staff of doctors caring for soldier patients, and will evaluate, promote, and improve, wherever possible, the quality of medical care given American soldiers.

The state committee on ophthalmology has recommended to the house of delegates of the Minnesota State Medical Association that an eye bank be established. This eye bank will be similar to the Eye Bank for Sight Restoration, Inc., in New York, and the one in Cook County Hospital, Chicago.

Each Thursday during October, Dr. Byron Smith gave a lecture on "Ophthalmic plastic surgery" at the Manhattan Eye, Ear, and Throat Hospital, 210 East 64th Street, New York 21.

La Sociedad Cubana de Oftalmologia is looking forward to the third Pan American Congress to be held in Havana in February, 1948, under the auspices of the Cuban government. A movement for the foundation of a League Against Blindness is headed by the wife of the president of the Republic. Work has already begun on a hospital for the treatment of eye diseases among the poor. The foundation stone of the building has been laid, and it is hoped the building will be finished and functioning perfectly by the time the Congress convenes in Havana.

The Alabama Sight Conservation Association has recently donated $10,000 to the Department of Ophthalmology of the Medical College of Alabama, to provide equipment for the University Eye Clinic. The Alabama Sight Conservation Association was originated and is sponsored by the Lions Clubs of Alabama.

SOCIETIES

Among the special guests taking part in the program of the American Academy of Ophthalmology and Otolaryngology at the Palmer House, Chicago, October 13th to 18th were: Dr. James B. Brown, St. Louis; Raymond Carhart, Ph.D., Evanston, Illinois; Mr. Howard Carter, Chicago; Helen Goodell, New York; Dr. Fremont C. Hall, Chester, Pennsylvania; Dr. Robison D. Harley, Atlantic City, New Jersey; Dr. Merrill B. Hayes, Chester, Pennsylvania; Dr. Horton C. Hinshaw, Rochester, Minnesota; Thomas H. Holmes, New York; Dr. James T. Mills, Dallas, Texas; Prof. W. J. B. Riddell, Scotland; Dr. Benjamin Rones, Washington, D.C.; Dr. L. von Sallmann, New York; Dr. C. L. Schepens, Brussels, Belgium;

Lieut. Col. Emory L. Shiflett, Cleveland; Dr. Frederick W. Stocker, Durham, North Carolina; Harold Westlake, Ph.D., Chicago; Helenor Campbell Wilder, Washington, D.C.; Dr. Stewart G. Wolf, Jr., New York; and Dr. Harold G. Wolff, New York.

The 1946 session, under the presidency of Dr. Gordon B. New, Rochester, Minnesota, had for its guest of honor, Dr. George M. Coates, Philadelphia. Dr. Curtis F. Burnam, Dr. Samuel J. Crowe, and Dr. Charles E. Iliff, Jr., all of Baltimore, presented a symposium on radiation therapy. Dr. Crowe's presentation was the Wherry Memorial Lecture.

The American Orthoptics Council had a joint session with the American Association of Orthoptic Technicians.

Personals

The following citation accompanied the award of the Legion of Merit to Dr. James N. Greear, Jr., 3532 Edmund Street, N.W., Washington, D.C. As a lieutenant colonel, Dr. Greear "rendered distinguished service as Chief of the Eye, Ear, Nose, and Throat Service, Valley Forge General Hospital, Phoenixville, Pennsylvania, from October, 1943, to February, 1945. Through his outstanding background, tact, and professional ability, Colonel Greear contributed greatly to facilitating the high standard of care rendered blind patients. . . ."

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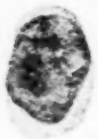

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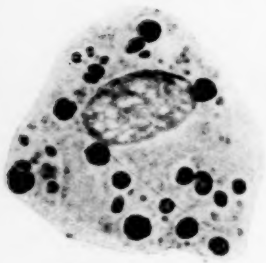

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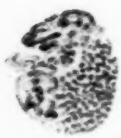

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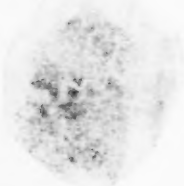

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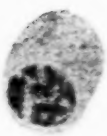

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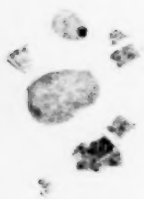

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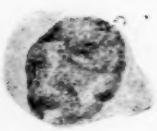
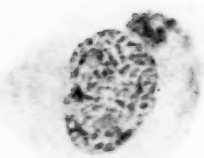


LARGE MONONUCLEAR CELL SHOWING FRAGMENTATION



PSEUDO INCLUSION BODY

DIPHTHEROID BACTERIA ON KERATINIZED EPITHELIAL CELL

-Belfie-

Cytology of Conjunctival Scrapings

PLATE 1 (THYGESON). CELLS FOUND IN CONJUNCTIVAL SCRAPINGS AND EXUDATES. GIEMSA STAIN. DRAWN FROM A MAGNIFICATION OF 1350.

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